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=> d his nofil

     (FILE 'HOME' ENTERED AT 16:33:12 ON 12 MAY 2006)

     FILE 'REGISTRY' ENTERED AT 16:33:23 ON 12 MAY 2006

     FILE 'HCAPLUS' ENTERED AT 16:33:24 ON 12 MAY 2006
                E PFEIFFER B/AU
L1           421 SEA ABB=ON  PLU=ON  ("PFEIFFER B"/AU OR "PFEIFFER B VICTOR"/AU)
                 OR "PFEIFFER BRUNO"/AU
                E PFEIFER B/AU
                E GINOT Y/AU
L2            13 SEA ABB=ON  PLU=ON  ("GINOT Y M"/AU OR "GINOT Y MICHEL"/AU OR
                "GINOT YVES MICHEL"/AU)
                E COQUEREL G/AU
L3            85 SEA ABB=ON  PLU=ON  ("COQUEREL G"/AU OR "COQUEREL GERARD"/AU)
                E BEILLES S/AU
L4             6 SEA ABB=ON  PLU=ON  ("BEILLES S"/AU OR "BEILLES STEPHANE"/AU)
L5           513 SEA ABB=ON  PLU=ON  (L1 OR L2 OR L3 OR L4)
L6             3 SEA ABB=ON  PLU=ON  L5 AND ?PERINDOPR?
L7             6 SEA ABB=ON  PLU=ON  (L1 AND (L2 OR L3 OR L4)) OR (L2 AND (L3
                OR L4)) OR (L3 AND L4)
L8             6 SEA ABB=ON  PLU=ON  (L6 OR L7)
L*** DEL      52 S L5 AND ?CRYSTALL?

     FILE 'REGISTRY' ENTERED AT 16:41:48 ON 12 MAY 2006
L9                STR
L10            4 SEA SSS SAM L9
L11          710 SEA SSS FUL L9

     FILE 'HCAPLUS' ENTERED AT 16:43:58 ON 12 MAY 2006
L12         1473 SEA ABB=ON  PLU=ON  L11
L13           19 SEA ABB=ON  PLU=ON  L12 AND (X-RAY OR X RAY OR (POWDER AND
                DIFFRAC?) OR CRYSTALL?)
L14            3 SEA ABB=ON  PLU=ON  L12 AND L5
L15            6 SEA ABB=ON  PLU=ON  L8 OR L14

     FILE 'REGISTRY' ENTERED AT 16:46:01 ON 12 MAY 2006
L16               STR
L17           12 SEA SUB=L11 SSS FUL L16
                D SCA
L18               STR L9
L19           59 SEA SUB=L11 SSS FUL L18

     FILE 'HCAPLUS' ENTERED AT 16:48:58 ON 12 MAY 2006
L20           84 SEA ABB=ON  PLU=ON  L17
L21          939 SEA ABB=ON  PLU=ON  L19
L22           84 SEA ABB=ON  PLU=ON  L20 AND L21
L23           84 SEA ABB=ON  PLU=ON  L17 AND L19
L24           16 SEA ABB=ON  PLU=ON  L23 AND (?CRYS? OR POWDER? OR DIFFRAC? OR
                XRAY?  OR X-RAY OR X(W)RAY)
L25           26 SEA ABB=ON  PLU=ON  L13 OR L24

     FILE 'REGISTRY' ENTERED AT 16:51:33 ON 12 MAY 2006
L26           11 SEA ABB=ON  PLU=ON  L17 AND L19
L27            3 SEA ABB=ON  PLU=ON  L26 AND NC<3
                D SCA

     FILE 'HCAPLUS' ENTERED AT 16:52:20 ON 12 MAY 2006
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L28           84 SEA ABB=ON  PLU=ON  L27
L29           13 SEA ABB=ON  PLU=ON  L28 NOT (PY>2000 OR AY>2000 OR PRY>2000)
L30           38 SEA ABB=ON  PLU=ON  L29 OR L25

=> fil hcap
FILE 'HCAPLUS' ENTERED AT 16:53:32 ON 12 MAY 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)
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FILE COVERS 1907 - 12 May 2006  VOL 144 ISS 21
FILE LAST UPDATED: 11 May 2006  (20060511/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> d que l30
L9              STR
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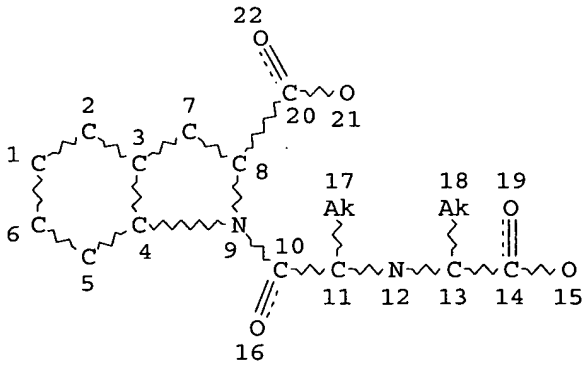


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NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  22

STEREO ATTRIBUTES: NONE
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L12         1473 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L11
L13           19 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L12 AND (X-RAY OR X RAY OR
                 (POWDER AND DIFFRAC?) OR CRYSTALL?)
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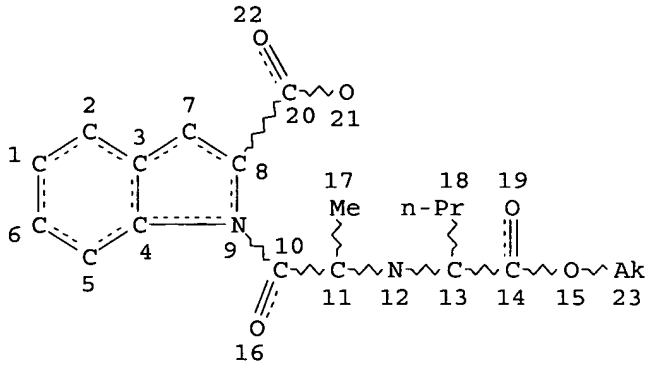
L16 STR

Ak~NH2
1 2

NODE ATTRIBUTES:
CONNECT IS E1 RC AT 1
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 2

STEREO ATTRIBUTES: NONE
L17 12 SEA FILE=REGISTRY SUB=L11 SSS FUL L16
L18 STR



NODE ATTRIBUTES:
CONNECT IS E3 RC AT 11
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CONNECT IS E1 RC AT 21
CONNECT IS E1 RC AT 23
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 23

STEREO ATTRIBUTES: NONE
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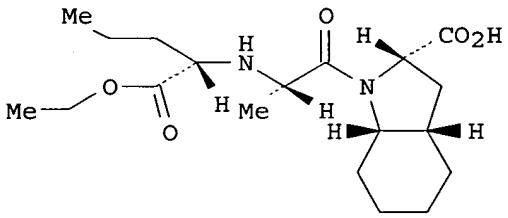
L23 84 SEA FILE=HCAPLUS ABB=ON PLU=ON L17 AND L19
L24 16 SEA FILE=HCAPLUS ABB=ON PLU=ON L23 AND (?CRYS? OR POWDER? OR DIFFRAC? OR XRAY? OR X-RAY OR X(W)RAY)
L25 26 SEA FILE=HCAPLUS ABB=ON PLU=ON L13 OR L24
L26 11 SEA FILE=REGISTRY ABB=ON PLU=ON L17 AND L19
L27 3 SEA FILE=REGISTRY ABB=ON PLU=ON L26 AND NC<3
L28 84 SEA FILE=HCAPLUS ABB=ON PLU=ON L27
L29 13 SEA FILE=HCAPLUS ABB=ON PLU=ON L28 NOT (PY>2000 OR AY>2000 OR PRY>2000)
L30 38 SEA FILE=HCAPLUS ABB=ON PLU=ON L29 OR L25

=> d l30 ibib abs hitstr 1-38

L30 ANSWER 1 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:356970 HCAPLUS
DOCUMENT NUMBER: 144:398255
TITLE: Preparation of hydrated **crystalline** forms of perindopril erbumine and pharmaceutical formulations
INVENTOR(S): Rucman, Rudolf; Zupet, Pavel
PATENT ASSIGNEE(S): Diagen Smartno Pri Ljubljani, d.o.o., Slovenia
SOURCE: 17 pp.
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1647547	A1	20060419	EP 2005-468015	20051013
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU				
PRIORITY APPLN. INFO.:			SI 2004-285 A	20041015

GI



I

AB The object of the invention are new **cryst**. forms perindopril erbumine (I.Me3CNH2) monohydrate, I.Me3CNH2 sesquihydrate and I.Me3CNH2 dihydrate and a process for the preparation thereof by dissolving I.Me3CNH2 in water or in water with the addition of a volatile water-miscible polar organic solvent, freezing and lyophilizing. Another object of the invention is a new process for the preparation of perindopril erbumine monohydrate in pure **cryst**. form by freezing aqueous acetone solns. and lyophilizing. Another object of the invention are pharmaceutical formulations for the treatment of arterial hypertension and with vasodilatory activity, containing a therapeutically effective amount of these new **cryst**. forms.

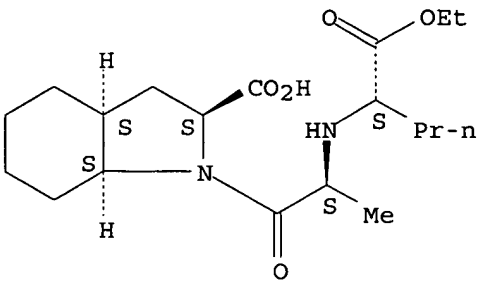
IT **107133-36-8**, Perindopril erbumine **690267-97-1** **882674-51-3** **882674-53-5**, Perindopril erbumine sesquihydrate
RL: CPS (Chemical process); PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(preparation of hydrated **cryst**. forms of perindopril erbumine and pharmaceutical formulations)

RN 107133-36-8 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

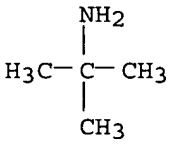
CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N

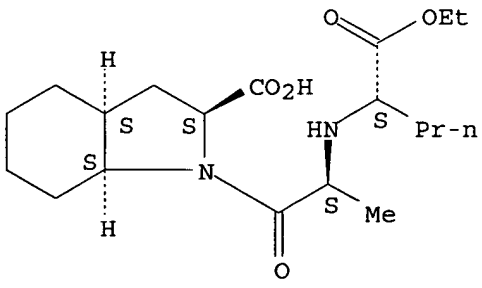


RN 690267-97-1 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1), monohydrate (9CI) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



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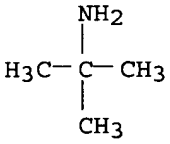
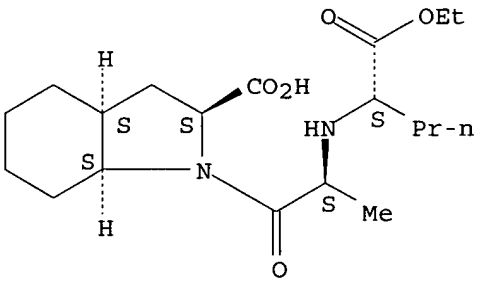


RN 882674-51-3 HCAPLUS
CN INDEX NAME NOT YET ASSIGNED

CM 1

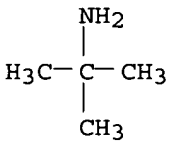
CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N

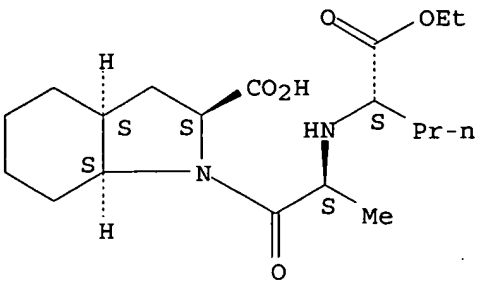


RN 882674-53-5 HCAPLUS
CN INDEX NAME NOT YET ASSIGNED

CM 1

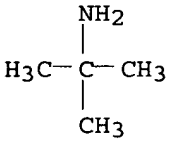
CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L30 ANSWER 2 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1201076 HCAPLUS
DOCUMENT NUMBER: 143:446810
TITLE: Processes for the preparation of alpha polymorph of perindopril erbumine
INVENTOR(S): Joshi, Narendra Shriram; Bhirud, Shekhar Bhaskar; Rao, Kodali Eswara
PATENT ASSIGNEE(S): Glenmark Pharmaceuticals Limited, India
SOURCE: U.S. Pat. Appl. Publ., 8 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005250706	A1	20051110	US 2005-122731	20050505
WO 2005108365	A1	20051117	WO 2005-IB1233	20050506

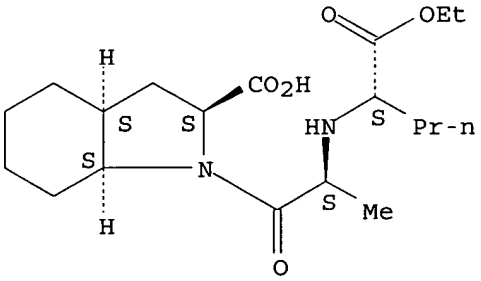
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,

MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: IN 2004-MU531 A 20040507
US 2004-572402P P 20040519
OTHER SOURCE(S): MARPAT 143:446810
AB A process for the preparation of an alpha polymorph of perindopril erbumine is provided comprising (a) forming a solution comprising perindopril erbumine in one or more ketones; (b) heating the solution to reflux; and (c) cooling the solution to a temperature sufficient to form the alpha polymorph of perindopril erbumine. The alpha polymorphs of perindopril erbumine obtained herein have a high purity level.
IT **107133-36-8P**, Perindopril erbumine
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(of perindopril erbumine α-polymorph)
RN 107133-36-8 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

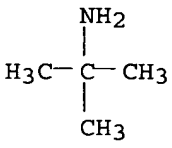
CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N



L30 ANSWER 3 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1103553 HCAPLUS
DOCUMENT NUMBER: 143:373364
TITLE: Process for preparing a solid pharmaceutical composition of perindopril

INVENTOR(S): Klobcar, Iztok; Puncuh-Kolar, Alesa; Grandovec, Anica; Turk, Urska; Solmajer-Lampic, Polona
PATENT ASSIGNEE(S): Krka, Tovarna Zdravil D.D. Novo Mesto, Slovenia
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005094793	A1	20051013	WO 2005-EP3277	20050329
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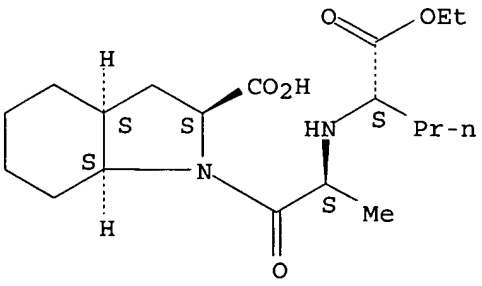
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 102004019845	A1	20051020	DE 2004-102004019845	20040329
PRIORITY APPLN. INFO.:			DE 2004-102004019845A	20040329
			DE 2004-102004059521A	20041209

AB The invention relates to a process for preparing a solid pharmaceutical composition of perindopril or a salt thereof which avoids a wet granulation step and results in very stable pharmaceutical compns., like tablets. A composition also comprises indapamide. For example, tablets were prepared by compression of a dry mixture comprising perindopril erbumine 4 mg, indapamide 1.25 mg, **microcryst**. cellulose 22.50 mg, lactose monohydrate 71.03 mg, sodium bicarbonate 0.50 mg, colloidal silica 0.27 mg, and magnesium stearate 0.45 mg.

IT **82834-16-0**, Perindopril **107133-36-8**, Perindopril erbumine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(perindopril solid compns. comprising carbonate stabilizer)

RN 82834-16-0 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



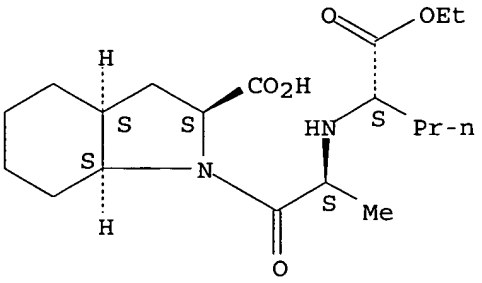
RN 107133-36-8 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

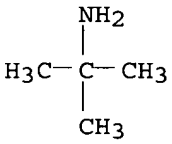
CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L30 ANSWER 4 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:673261 HCAPLUS
DOCUMENT NUMBER: 143:153713
TITLE: New **crystalline** form of perindopril
INVENTOR(S): Rucman, Rudolf
PATENT ASSIGNEE(S): Lek Pharmaceuticals D. D., Slovenia
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005068425	A1	20050728	WO 2005-EP283	20050113

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LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
MR, NE, SN, TD, TG

SI 21704 C 20050831 SI 2004-12 20040114
PRIORITY APPLN. INFO.: SI 2004-12 A 20040114
OTHER SOURCE(S): CASREACT 143:153713

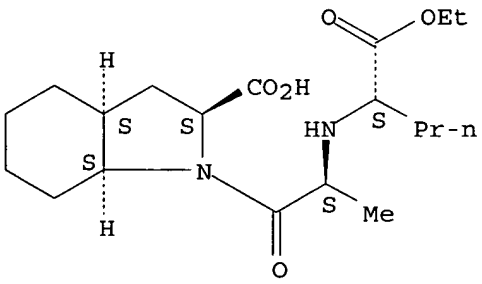
AB The invention relates to a process for the preparation of ACE inhibitor perindopril which starts from N-[(S)-1-carbethoxybutyl]-L-alanine and involves trimethylsilyl protection and conversion to reactive acid chloride for reaction with (2S,3aS,7aS)-octahydroindole-2-carboxylic acid having a protected carboxyl group. The invention also relates to new **cryst**. and amorphous forms of perindopril. Thus, perindopril obtained by reaction of silylated reactants was purified by filtering a CH2Cl2 solution through a silica gel column and **crystg**. from an Et ether solution Perindopril in new **cryst**. form (78.2%) was obtained.

IT **82834-16-0P**, Perindopril
RL: IMF (Industrial manufacture); PRP (Properties); PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(**crystal** structure; preparation of perindopril in new **cryst**. form)

RN 82834-16-0 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT **107133-36-8P**, Perindopril erbumine
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of perindopril in new **cryst**. form)

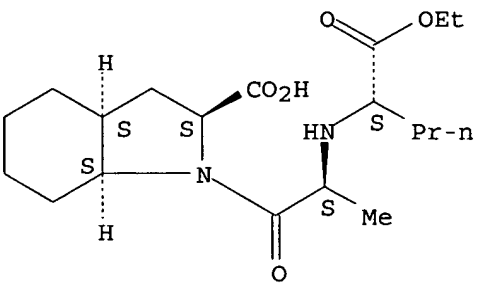
RN 107133-36-8 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

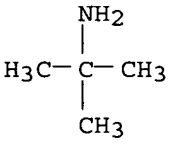
CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



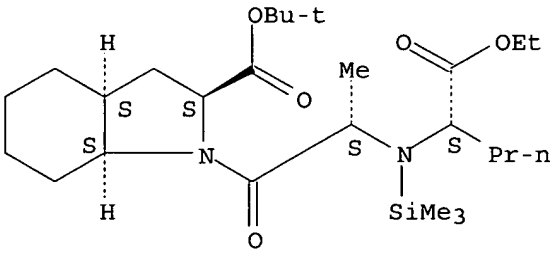
CM 2

CRN 75-64-9
CMF C4 H11 N



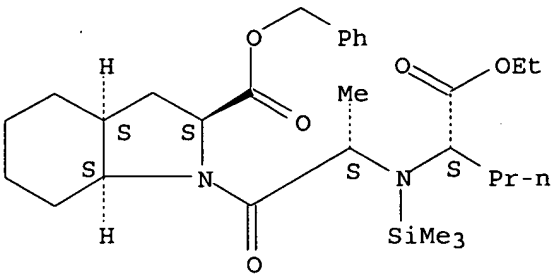
IT **859511-85-6P 861818-61-3P 861818-65-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of perindopril in new **cryst**. form)
RN 859511-85-6 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl](trimethylsilyl)amino]-1-oxopropyl]octahydro-, 1,1-dimethylethyl ester, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



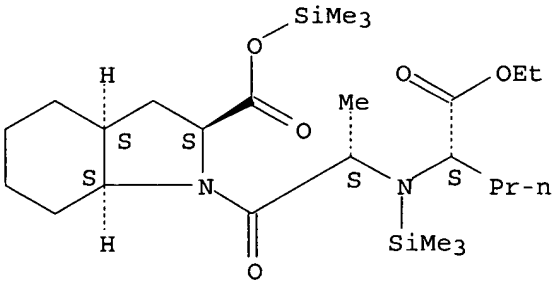
RN 861818-61-3 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl](trimethylsilyl)amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 861818-65-7 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl](trimethylsilyl)amino]-1-oxopropyl]octahydro-, trimethylsilyl ester, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L30 ANSWER 5 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:493585 HCAPLUS
DOCUMENT NUMBER: 143:32341
TITLE: Method for producing {N-[1-(S)-carbalkoxy-3-phenylpropyl]-S-alanyl-2S, 3aR, 7aS-octahydroindol-2-carboxylic acid} compounds especially trandolapril via their racemic salts
INVENTOR(S): Pogutter, Mirko; Rudolf, Felix; Bichsel, Hans-Ulrich; Bader, Thomas
PATENT ASSIGNEE(S): Azad Pharmaceuticals Ingredients A.-G., Switz.
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005051909	A1	20050609	WO 2004-CH688	20041115

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,

TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: CH 2003-2038 A 20031128

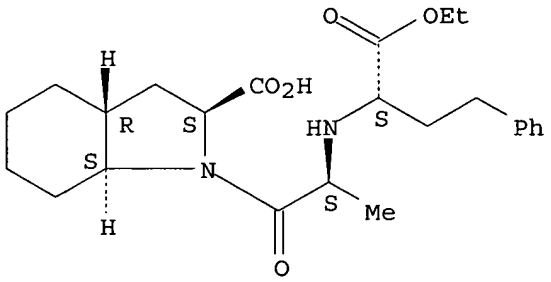
AB The invention relates to a method for producing optionally substituted {N-[1-(S)-carbalkoxy-3-phenylpropyl]-S-alanyl-2S, 3aR, 7aS-octahydroindol-2-carboxylic acid} and the pharmaceutically acceptable salts thereof. To this end, a racemic mixture of optionally substituted trans-octahydroindol-2-carboxylic acid is reacted with the N-carboxyanhydride of {N-[1-(S)-alkoxycarbonyl-3-phenylpropyl]-L-alanine}, which is optionally substituted on the Ph ring, in an appropriate inert solvent, and the obtained optionally substituted {N-[1-(S)-carbalkoxy-3-phenylpropyl]-S-alanyl-2S, 3aR, 7aS-octahydroindol-2-carboxylic acid}, preferably trandolapril, is subsequently isolated, as well as polymorphous forms A and B of trandolapril.

IT **87725-72-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(method for producing {N-[1-(S)-carbalkoxy-3-phenylpropyl]-S-alanyl-2S, 3aR, 7aS-octahydroindol-2-carboxylic acid} compds. especially trandolapril via their racemic salts)

RN 87725-72-2 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, monohydrochloride, (2S,3aR,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



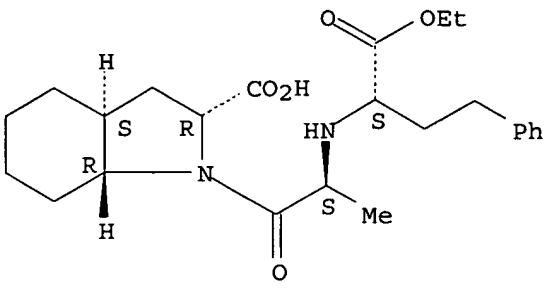
● HCl

IT **852921-57-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(method for producing {N-[1-(S)-carbalkoxy-3-phenylpropyl]-S-alanyl-2S, 3aR, 7aS-octahydroindol-2-carboxylic acid} compds. especially trandolapril via their racemic salts)

RN 852921-57-4 HCAPLUS

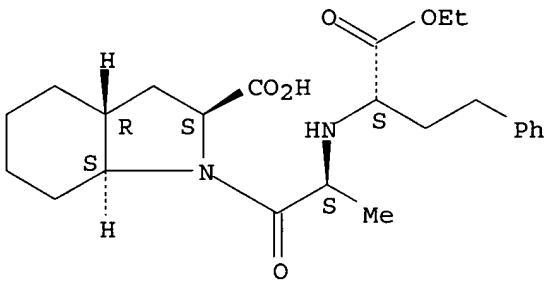
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2R,3aS,7aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **87679-37-6P**, Trandolapril
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(method for producing {N-[1-(S)-carbalkoxy-3-phenylpropyl]-S-alanyl-2S, 3aR, 7aS-octahydroindol-2-carboxylic acid} compds. especially trandolapril via their racemic salts)
RN 87679-37-6 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aR,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

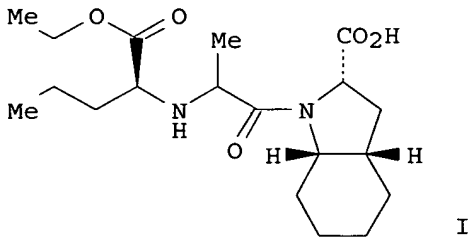
L30 ANSWER 6 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:371219 HCAPLUS
DOCUMENT NUMBER: 142:435775
TITLE: Novel method for preparation of **crystalline** perindopril erbumine
INVENTOR(S): Singh, Girij Pal; Godbole, Himanshu Madhav; Nehate, Sagar Purushottam
PATENT ASSIGNEE(S): Lupin Ltd., India
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005037788	A1	20050428	WO 2003-IN340	20031021

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE,
GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,
LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,
OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2003300689 A1 20050505 AU 2003-300689 20031021
PRIORITY APPLN. INFO.: WO 2003-IN340 A 20031021
GI



I

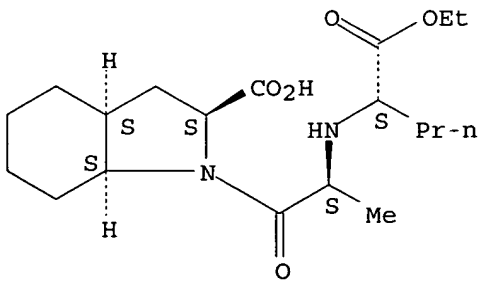
AB **Cryst**. perindopril erbumine (I.H2NBu-tert) is prepared and the **x-ray** (**powder**) **diffraction** pattern given. The process comprises reacting a solution of perindopril (I), in a solvent selected from DMF or di-Me acetals of lower aliphatic aldehydes and ketones with tertiary butylamine and **crystn**. of the erbumine salt thus obtained by heating the reaction mixture to reflux, filtering hot, cooling gradually to 20-30°, and further cooling to 0-15° for 30 min-1 h and finally filtering off and drying the **crystals**.

IT **82834-16-0P**, Perindopril
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of **cryst**. perindopril erbumine)

RN 82834-16-0 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

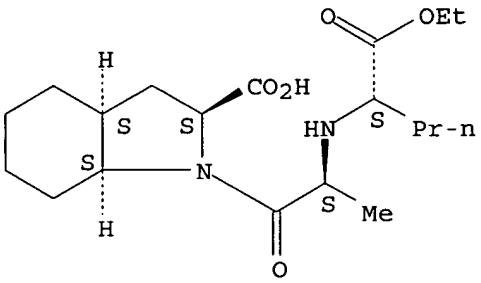


IT **107133-36-8P**, Perindopril erbumine
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of **cryst**. perindopril erbumine)
RN 107133-36-8 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

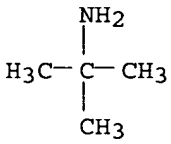
CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



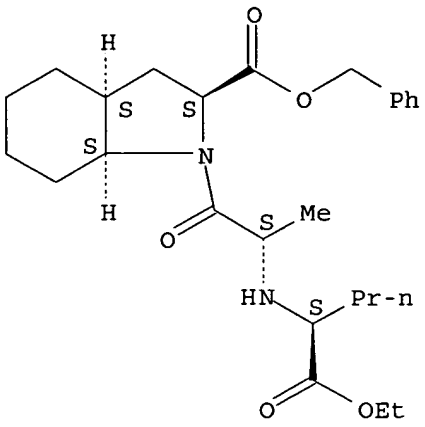
CM 2

CRN 75-64-9
CMF C4 H11 N



IT **122454-52-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of **cryst**. perindopril erbumine)
RN 122454-52-8 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L30 ANSWER 7 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:1154670 HCAPLUS
DOCUMENT NUMBER: 142:62765
TITLE: Preparation of various **crystalline** forms of perindopril erbumine for use as drug
INVENTOR(S): Straessler, Christoph; Lellek, Vit; Faessler, Roger
PATENT ASSIGNEE(S): Azad Pharmaceutical Ingredients AG, Switz.
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004113293	A1	20041229	WO 2004-CH374	20040618
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2530550	AA	20041208	CA 2004-2530550	20040618
AU 2004249345	A1	20041229	AU 2004-249345	20040618
EP 1636185	A1	20060322	EP 2004-737029	20040618
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				

PRIORITY APPLN. INFO.: CH 2003-1109 A 20030624
WO 2004-CH374 W 20040618

AB Disclosed are two novel **cryst**. forms d and e of perindopril erbumine, which are suitable as therapeutic substances in medicaments used for treating cardiovascular diseases, especially high blood pressure and cardiac

insufficiency. **Cryst**. form e is obtained by **crystg**. perindopril erbumine from MTBE containing 1.5 to 2.5 % (volume/volume) of water at 30 to 45°, preferably 34 to 45°, **crystn**. expediently taking place by stirring. **Cryst**. form e changes into **cryst**. form d if the water is removed, practically by azeotropic distillation, preferably at 35 to 37°, and stirring continues for at least 15 h at 30 to 45°, preferably 35 to 37°. **Cryst**. form d can also be obtained by stirring **cryst**. form a or ss in tert-Bu Me ether containing 0.9 to 1.4 % (volume/volume) of water at 33 to 38° while inoculating the same with **cryst**. form d. **Cryst**. form e can further be obtained by stirring **cryst**. form a or ss in tert-Bu Me ether containing 0.9 to 1.4 % (volume/volume) of water at 28 to 35° while inoculating the same with **cryst**. form e, or by stirring **cryst**. form a or ss in tert-Bu Me ether containing 1.5 to 2.0 % (volume/volume) of water at 35 to 38°.

IT **107133-36-8**, Perindopril erbumine
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(preparation of various **cryst**. forms of perindopril erbumine for use as drug)

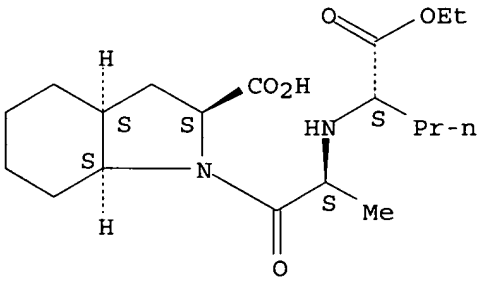
RN 107133-36-8 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

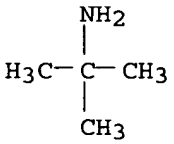
CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L30 ANSWER 8 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:740299 HCAPLUS
DOCUMENT NUMBER: 141:248754
TITLE: Novel **crystalline** forms of trandolapril
INVENTOR(S): Parthasaradhi, Reddy Bandi; Rathnakar, Reddy Kura; Raji, Reddy Rapolu; Narasa, Reddy Bolla; Muralidhara, Reddy Dasari
PATENT ASSIGNEE(S): Hetero Drugs Limited, India
SOURCE: PCT Int. Appl., 14 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

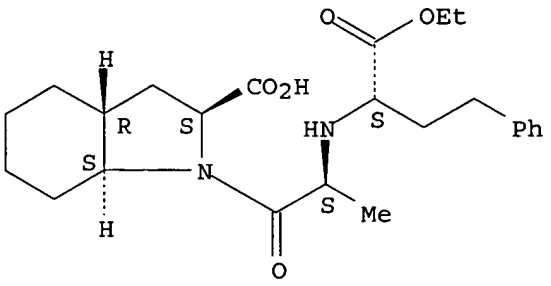
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004076417	A1	20040910	WO 2003-IN38	20030227
WO 2004076417	C2	20050804		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003209670	A1	20040917	AU 2003-209670	20030227
EP 1597230	A1	20051123	EP 2003-742857	20030227
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2004220252	A1	20041104	US 2003-250654	20030703
PRIORITY APPLN. INFO.:			WO 2003-IN38 A	20030227

AB The present invention relates to 2 novel **cryst**. polymorphs of trandolapril, processes for their preparation and pharmaceutical compns. containing them. Trandolapril was prepared and dissolved in EtOAc and refluxed for 30 min. The solution was cooled to 20-25° and the crystals obtained were dried to give a form II **cryst**. polymorph of trandolapril.

IT **87679-37-6P**, Trandolapril
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of **cryst**. forms of trandolapril)

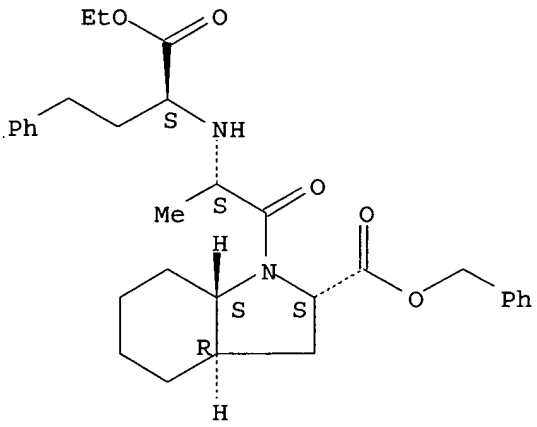
RN 87679-37-6 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aR,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT **98677-37-3**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of **cryst**. forms of trandolapril)
RN 98677-37-3 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aR,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L30 ANSWER 9 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:676310 HCAPLUS
DOCUMENT NUMBER: 141:238870
TITLE: Inhibition of angiotensin I-converting enzyme induces radioprotection by preserving murine hematopoietic short-term reconstituting cells
AUTHOR(S): Charrier, Sabine; Michaud, Annie; Badaoui, Sabrina; Giroux, Sebastien; Ezan, Eric; Sainteny, Francoise; Corvol, Pierre; Vainchenker, William
CORPORATE SOURCE: Institut National de la Sante et de la Recherche Medicale (INSERM), Hematopoiese et Cellules Souches, Institut Gustave Roussy, Villejuif, Fr.
SOURCE: Blood (2004), 104(4), 978-985
CODEN: BLOOAW; ISSN: 0006-4971

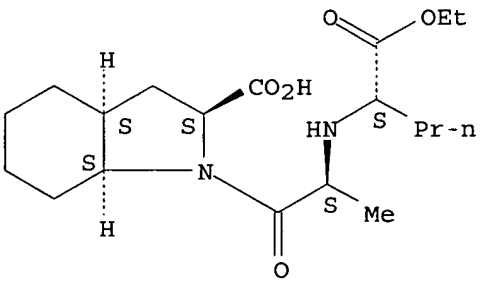
PUBLISHER: American Society of Hematology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Angiotensin I-converting enzyme (ACE) inhibitors can affect hematopoiesis by several mechanisms including inhibition of angiotensin II formation and increasing plasma concns. of AcSDKP (acetyl-N-Ser-Asp-Lys-Pro), an ACE substrate and a neg. regulator of hematopoiesis. We tested whether ACE inhibition could decrease the hematopoietic toxicity of lethal or sublethal irradiation protocols. In all cases, short treatment with the ACE inhibitor perindopril protected against irradiation-induced death. ACE inhibition accelerated hematopoietic recovery and led to a significant increase in platelet and red cell counts. Pretreatment with perindopril increased bone marrow cellularity and the number of hematopoietic progenitors (granulocyte macrophage colony-forming unit [CFU-GM], erythroid burst-forming unit [BFU-E], and megakaryocyte colony-forming unit [CFU-MK]) from day 7 to 28 after irradiation Perindopril also increased the number of hematopoietic stem cells with at least a short-term reconstitutive activity in animals that recovered from irradiation To determine the mechanism of action involved, we evaluated the effects of increasing AcSDKP plasma concns. and of an angiotensin II type 1 (AT1) receptor antagonist (telmisartan) on radioprotection. We found that the AT1-receptor antagonism mediated similar radioprotection as the ACE inhibitor. These results suggest that ACE inhibitors and AT1-receptor antagonists could be used to decrease the hematopoietic toxicity of irradiation

IT **82834-16-0**, Perindopril
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ACE inhibition induces radioprotection by preserving hematopoietic short-term reconstituting cells)

RN 82834-16-0 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L30 ANSWER 10 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:633914 HCAPLUS
DOCUMENT NUMBER: 141:140316
TITLE: Process for producing intermediate for trandolapril by esterification of racemic (2S,3aR,7aS)-hexahydroindoline-2-carboxylic acid with benzyl alcohol and optical resolution

INVENTOR(S): Shimamura, Hiroshi; Nakata, Yoshitaka
PATENT ASSIGNEE(S): Ohara Chemical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004065368	A1	20040805	WO 2004-JP374	20040119

W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GH, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ

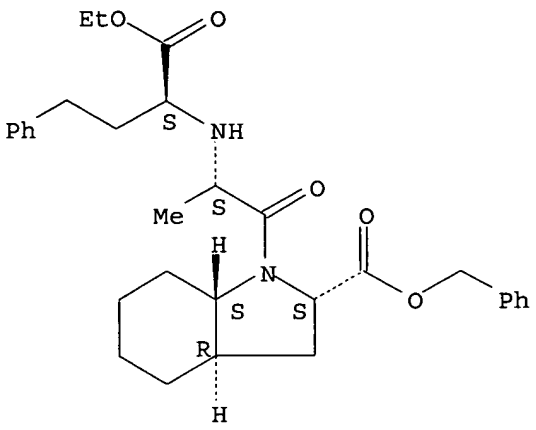
PRIORITY APPLN. INFO.: JP 2003-11889 A 20030121
OTHER SOURCE(S): CASREACT 141:140316

AB Disclosed is a process for producing benzyl (2S,3aR,7aS)-hexahydroindoline-2-carboxylate (I), characterized by heating a racemic mixture consisting of (2S,3aR,7aS)-hexahydroindoline-2-carboxylic acid (II) and (2R,3aS,7aR)-hexahydroindoline-2-carboxylic acid (III), benzyl alc., and optically active 10-camphorsulfonic acid in a nonaq. solvent to convert the racemic mixture to benzyl esters, subjecting the diastereomeric salts of the benzyl esters with the optically active 10-camphorsulfonic acid which have been generated in the same reaction system to optical resolution based on a difference in solubility in an organic solvent, and then treating one of the isomers with a base. This process can simultaneously carry out esterification of a mixture of racemic II and III with benzyl alc. and optical resolution in one step in high yield, shortens the existing process by two steps, and is industrially advantageous. Thus, a racemic mixture of II and III 67.69, benzyl alc. 129.77, and (1R)-(-)-10-camphorsulfonic acid (IV) 97.57 g were added to toluene in a flask fitted with a condenser and a Dean-Stark separator, refluxed with stirring while removing a theor. quantity of water, distilled under reduced pressure to remove the solvent (.apprx.650 mL), and treated with 800 mL tert-Bu Me ether at .apprx.60° with stirring. The precipitated crystals were collected by filtration, successively washed with toluene and tert-Bu Me ether , dried to give a crude **cryst**. diastereomer salt (189.5 g) which was recrystd. twice from toluene to give the diastereomer I.IV salt (63.5 g) which was added to a mixture of 315 mL tert-Bu Me ether and 63 mL H2O, treated dropwise with 130 mL 10.6% aqueous Na2CO3 solution, stirred for 10 min to give, after workup, 33.2 g I (64.0% from the racemate).

IT **98677-37-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of optically active benzyl (2S,3aR,7aS)-hexahydroindolinecarboxylate as intermediate for trandolapril by esterification of racemic (2SR,3aRS,7aSR)-hexahydroindolinecarboxylic acid and optical resolution using camphorsulfonic acid)

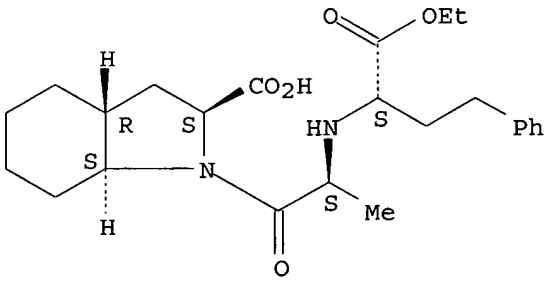
RN 98677-37-3 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aR,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **87679-37-6P**, Trandolapril
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of optically active benzyl (2S,3aR,7aS)-hexahydroindolinecarboxylate as intermediate for trandolapril by esterification of racemic (2SR,3aRS,7aSR)-hexahydroindolinecarboxylic acid and optical resolution using camphorsulfonic acid)
RN 87679-37-6 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aR,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



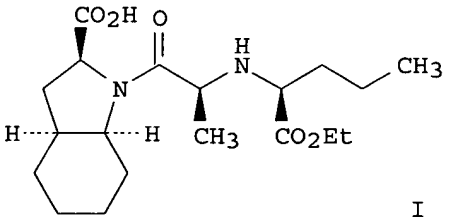
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L30 ANSWER 11 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:405692 HCAPLUS
DOCUMENT NUMBER: 140:407109
TITLE: Hydrogenolysis of benzyl ester of perindopril for preparing perindopril monohydrates for use as inhibitors of angiotensin converting enzyme (ACE)
INVENTOR(S): Rao, Dharmaraj Ramachandra; Kankan, Rajendra Narayanrao
PATENT ASSIGNEE(S): Cipla Limited, India
SOURCE: Brit. UK Pat. Appl., 16 pp.
CODEN: BAXXDU

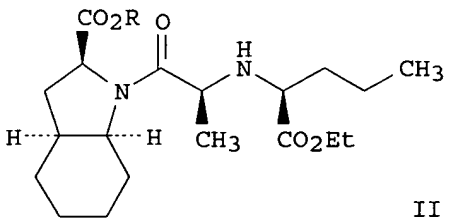
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2395195	A1	20040519	GB 2002-26885	20021118
CA 2506587	AA	20040603	CA 2003-2506587	20031118
WO 2004046172	A1	20040603	WO 2003-GB4981	20031118
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003283588	A1	20040615	AU 2003-283588	20031118
EP 1565485	A1	20050824	EP 2003-775565	20031118
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003015703	A	20051025	BR 2003-15703	20031118
CN 1738830	A	20060222	CN 2003-80108700	20031118
US 2006063941	A1	20060323	US 2005-535187	20051031
PRIORITY APPLN. INFO.:			GB 2002-26885 A	20021118
			WO 2003-GB4981 W	20031118

OTHER SOURCE(S): CASREACT 140:407109; MARPAT 140:407109
GI



I



II

AB Perindopril (I), or a pharmaceutically acceptable salt thereof, may be prepared from a protected ester II (R = aralkyl, CH2Ph) via hydrogenolysis in the presence of a noble metal catalyst, such as Pd/charcoal, in the presence of a base. For example, when the base is tert-butylamine, it forms a pharmaceutically-acceptable addition salt with I, thus forming perindopril erbumine, I·tert-butylamine salt. A monohydrate of I, or a pharmaceutically acceptable salt thereof, is also claimed and may be prepared by hydrating I, or a pharmaceutically acceptable salt thereof, by way of addition of water or by drying in air. Perindopril erbumine monohydrate was prepared and studied by **x-ray diffraction**. Perindopril monohydrates may be used as angiotensin converting enzyme (ACE) inhibitors.

IT **690267-97-1P**, Perindopril erbumine monohydrate
RL: IMF (Industrial manufacture); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP

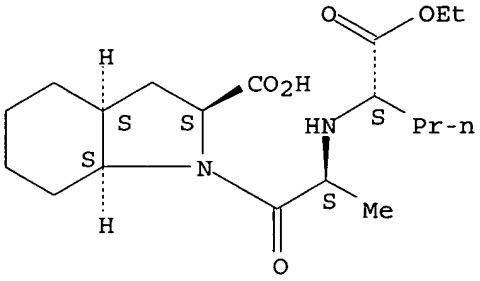
(Preparation); USES (Uses)
(**crystal** structure; preparation of perindopril, its salts and monohydrates from hydrogenolysis of its benzyl ester)

RN 690267-97-1 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1), monohydrate (9CI) (CA INDEX NAME)

CM 1

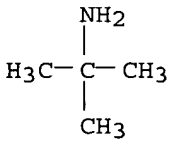
CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

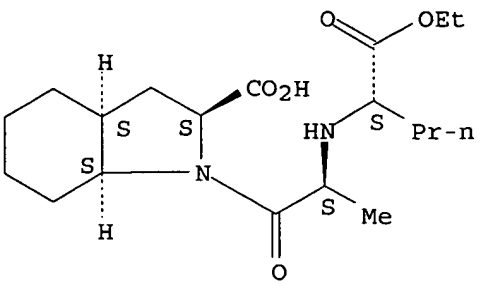
CRN 75-64-9
CMF C4 H11 N



IT **82834-16-0P**, Perindopril
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of perindopril, its salts and monohydrates from hydrogenolysis of its benzyl ester)

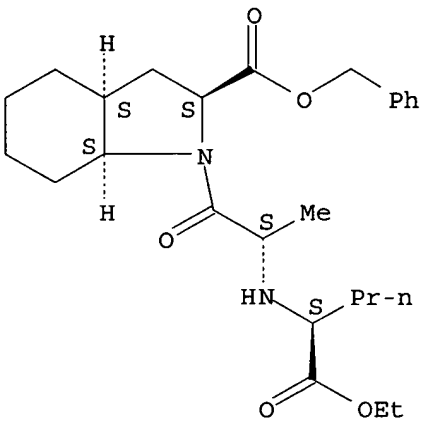
RN 82834-16-0 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT **122454-52-8**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of perindopril, its salts and monohydrates from hydrogenolysis of its benzyl ester)
RN 122454-52-8 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

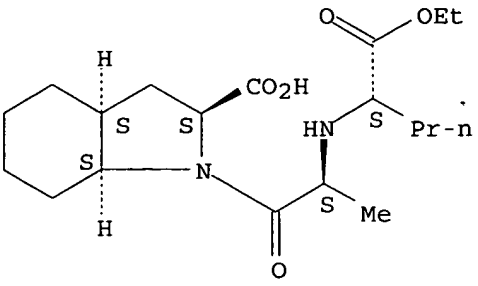


IT **107133-36-8P**, Perindopril erbumine
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of perindopril, its salts and monohydrates from hydrogenolysis of its benzyl ester)
RN 107133-36-8 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

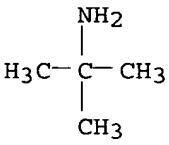
CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L30 ANSWER 12 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:363685 HCAPLUS
DOCUMENT NUMBER: 140:380637
TITLE: Stabilisation of pharmaceutical compositions comprising ACE inhibitor by absence of acidic excipients having large specific surface area, e.g. silicon dioxide
INVENTOR(S): Bergman, Jeffrey; Mantri, Pranita S.
PATENT ASSIGNEE(S): Niche Generics Limited, UK; Unichem Laboratories Limited
SOURCE: Brit. UK Pat. Appl., 50 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2394660	A1	20040505	GB 2003-29232	20031217
PRIORITY APPLN. INFO.:			GB 2003-29232	20031217

OTHER SOURCE(S): MARPAT 140:380637

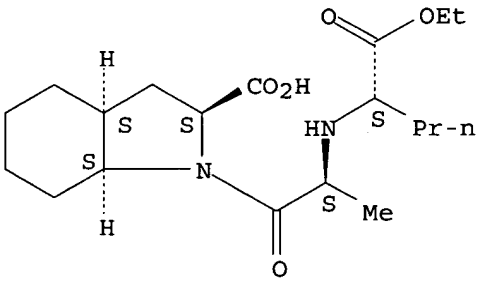
AB The present invention relates to stable pharmaceutical compns. comprising an ACE inhibitor (which are otherwise susceptible to degradation due to cyclisation, hydrolysis and oxidation). This is achieved by providing compns. substantially free of any acidic excipients having a large sp. surface area, especially substantially free of colloidal silicon dioxide. The composition also comprises one or more excipients, which are preferably compatible with the ACE inhibitor. The ACE inhibitor is preferably perindopril or ramipril. The composition may be used as a medicament for the

treatment or prevention of a cardiovascular disorder, hypertension, coronary heart disease or a cerebrovascular disease. The composition may further comprise a β-blocker, a diuretic, a calcium-channel blocker, a vasodilator anti- hypertensive drug, or an angiotensin II receptor antagonist.

IT **82834-16-0**, Perindopril **107133-36-8**, Perindopril erbumine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stabilization of pharmaceutical compns. comprising ACE inhibitor by absence of acidic excipients having large sp. surface area like silicon dioxide)

RN 82834-16-0 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

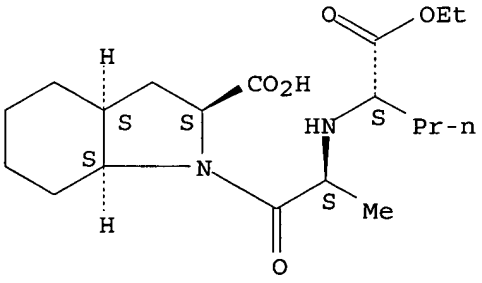


RN 107133-36-8 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

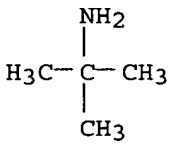
CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L30 ANSWER 13 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:120696 HCAPLUS
DOCUMENT NUMBER: 140:169624
TITLE: Pharmaceutical formulations comprising highly soluble drugs
INVENTOR(S): Vaya, Navin; Karan, Rajesh Singh; Nadkarni, Sunil Sadanand
PATENT ASSIGNEE(S): Torrent Pharmaceuticals Limited, India
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004012699	A2	20040212	WO 2003-IN261	20030801
WO 2004012699	A3	20040401		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003274680	A1	20040223	AU 2003-274680	20030801

PRIORITY APPLN. INFO.:

IN 2002-MU696	A	20020805
IN 2002-MU698	A	20020805
IN 2003-MU81	A	20030122
WO 2003-IN261	W	20030801

AB The present invention provides a novel modified release dosage form comprising a highly soluble drug, which utilizes dual retard technique to effectively reduce the quantity of release controlling agents and a process for preparing the dosage form. Specifically, the dosage form comprises micro matrix particles containing a highly soluble drug and one or more hydrophobic release controlling agents and coated micro matrix particles with one or more hydrophobic release controlling agents. The invention also relates to the use of dual retard technique to effectively control the release rate of modified release active ingredient by using small quantity of release controlling agents. The invention also provides a novel process for preparing the novel formulations of the invention. The invention further provides a method of treating an animal, particularly a

human in need of treatment utilizing the active agents, comprising administering a therapeutically effective amount of composition or solid oral dosage form according to the invention to provide administration of active ingredients.

IT **107133-36-8**, Perindopril erbumine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical formulations comprising highly soluble drugs)

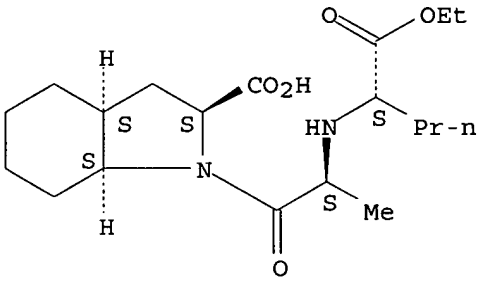
RN 107133-36-8 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

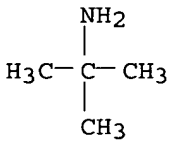
CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N



L30 ANSWER 14 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:1007353 HCAPLUS
DOCUMENT NUMBER: 140:47547
TITLE: Microcapsules for delayed and controlled release of perindopril
INVENTOR(S): Huet de Barochez, Bruno; Wuthrich, Patrick; Legrand, Valerie; Castan, Catherine; Meyrueix, Remi
PATENT ASSIGNEE(S): Les Laboratoires Servier, Fr.
SOURCE: Fr. Demande, 26 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2841140	A1	20031226	FR 2002-7778	20020624
FR 2841140	B1	20041001		
CA 2491172	AA	20031231	CA 2003-2491172	20030624
WO 2004000286	A1	20031231	WO 2003-FR1931	20030624
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003260620	A1	20040106	AU 2003-260620	20030624
BR 2003012026	A	20050322	BR 2003-12026	20030624
EP 1515704	A1	20050323	EP 2003-760778	20030624
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005533079	T2	20051104	JP 2004-514980	20030624
NO 2005000163	A	20050112	NO 2005-163	20050112
PRIORITY APPLN. INFO.:			FR 2002-7778 A	20020624
			WO 2003-FR1931 W	20030624

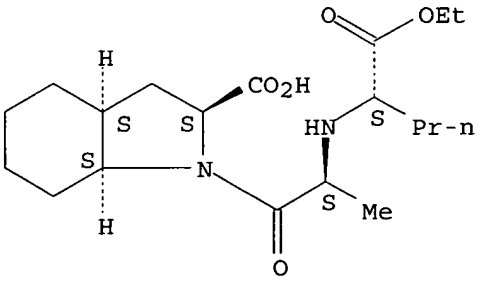
AB Microcapsules allowing the delayed and controlled release of perindopril, or one of its salts, intended for oral administration is prepared Microcapsules were made from tert-butylamine perindopril 700, Eudargit L100 37, and hydrogenated palm oil 56 g and their dissoln. rates were studied.

IT **82834-16-0**, Perindopril **107133-36-8 612548-45-5**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(microcapsules for delayed and controlled release of perindopril)

RN 82834-16-0 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



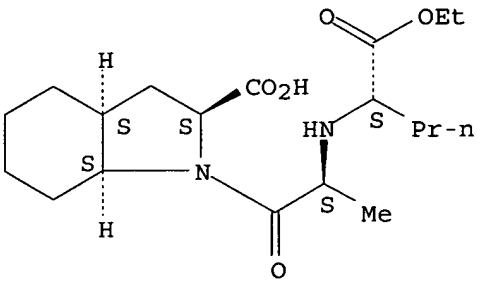
RN 107133-36-8 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

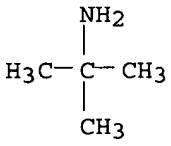
CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N

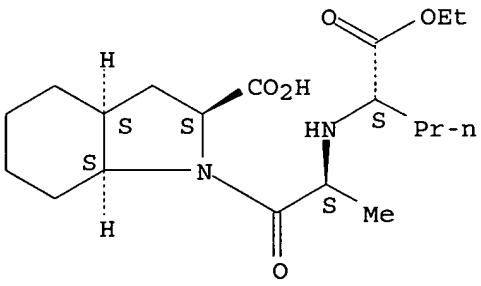


RN 612548-45-5 HCAPLUS
CN L-Arginine, mono[(2S,3aS,7aS)-1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylate] (9CI) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

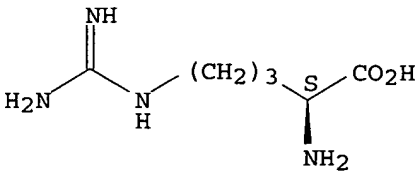
Absolute stereochemistry. Rotation (-).



CM 2

CRN 74-79-3
CMF C6 H14 N4 O2

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L30 ANSWER 15 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:754995 HCAPLUS
DOCUMENT NUMBER: 137:268473
TITLE: Porous drug matrices and methods of manufacture thereof
INVENTOR(S): Straub, Julie; Altreuter, David; Bernstein, Howard; Chickering, Donald E.; Khattak, Sarwat; Randall, Greg
PATENT ASSIGNEE(S): Acusphere Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 20 pp., Cont.-in-part of U. S. 6,395,300.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002142050	A1	20021003	US 2002-53929	20020122
US 6395300	B1	20020528	US 1999-433486	19991104
EP 1642572	A1	20060405	EP 2005-27194	20000525
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
US 6645528	B1	20031111	US 2000-694407	20001023
US 6932983	B1	20050823	US 2000-706045	20001103
ZA 2001010347	A	20030730	ZA 2001-10347	20011218
US 2005048116	A1	20050303	US 2004-924642	20040824
US 2005058710	A1	20050317	US 2004-928886	20040827

PRIORITY APPLN. INFO.:	US 1999-136323P	P	19990527
	US 1999-158659P	P	19991008
	US 1999-433486	A2	19991104
	US 2000-186310P	P	20000302
	EP 2000-939365	A3	20000525
	US 2002-53929	A3	20020122

AB Drugs, especially low aqueous solubility drugs, are provided in a porous matrix form, preferably microparticles, which enhances dissoln. of the drug in aqueous media. The drug matrixes preferably are made using a process that includes (i) dissolving a drug, preferably a drug having low aqueous solubility, in a volatile solvent to form a drug solution, (ii) combining at least one pore forming agent with the drug solution to form an emulsion, suspension, or

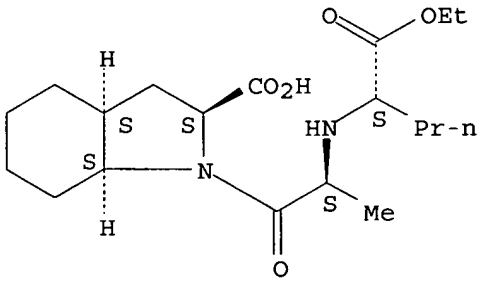
second solution and hydrophilic or hydrophobic excipients that stabilize the drug and inhibit **crystn**., and (iii) removing the volatile solvent and pore forming agent from the emulsion, suspension, or second solution to yield the porous matrix of drug. Hydrophobic or hydrophilic excipients may be selected to stabilize the drug in **cryst**. form by inhibiting crystal growth or to stabilize the drug in amorphous form by preventing **crystn**. The pore forming agent can be either a volatile liquid that is immiscible with the drug solvent or a volatile solid compound, preferably a volatile salt. In a preferred embodiment, spray drying is used to remove the solvents and the pore forming agent. The resulting porous matrix has a faster rate of dissoln. following administration to a patient, as compared to non-porous matrix forms of the drug. In a preferred embodiment, microparticles of the porous drug matrix are reconstituted with an aqueous medium and administered parenterally, or processed using standard techniques into tablets or capsules for oral administration. Thus, 5.46 g of PEG 8000, 0.545 g of prednisone, and 0.055 g of Span 40 were dissolved in 182 mL of methylene chloride. A solution of 3.27 g of ammonium bicarbonate in 18.2 mL of water was added to the organic solution (phase ratio 1:10) and homogenized for 5 min at 16,000 RPM.

The resulting emulsion was spray dried on a benchtop spray dryer using an air-atomizing nozzle and nitrogen as the drying gas.

IT **82834-16-0**, Perindopril **87679-37-6**, Trandolapril
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(porous drug matrixes and methods of manufacture thereof)

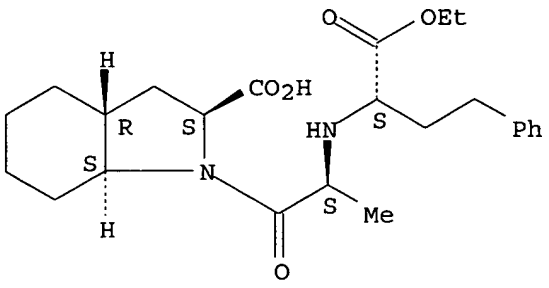
RN 82834-16-0 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 87679-37-6 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aR,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



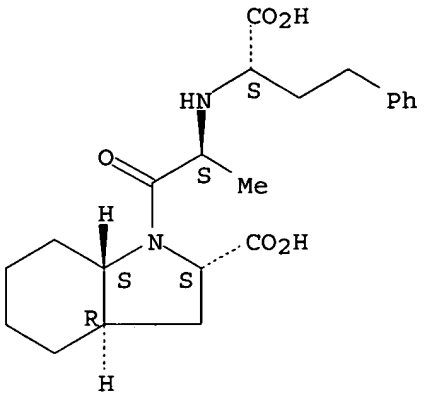
L30 ANSWER 16 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:445439 HCAPLUS
DOCUMENT NUMBER: 137:262634
TITLE: Preferred conformation of selected ACE inhibitors for interaction with ACE active site
AUTHOR(S): Smiesko, M.; Remko, M.
CORPORATE SOURCE: Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Comenius University, Bratislava, SK-832 32, Slovakia
SOURCE: Chemical Papers (2002), 56(2), 138-143
CODEN: CHPAEG; ISSN: 0366-6352
PUBLISHER: Slovak Academic Press Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Theor. methods were used to study structural properties of most common angiotensin-converting enzyme inhibitors (ACEIs): captopril, enalapril, perindopril, ramipril, benazepril, trandolapril, and cilazapril. In the first step, the active metabolites of ACEIs were modeled and all atoms were parametrized by extended MM2 parametrization set. Next, thorough conformational anal. was performed on all rotatable bonds, except those of 3-phenylpropyl or Bu fragment, which were set to low-energy (all-trans) extended arrangement. The values of dihedral angles were varied over the range of 360° in 15° increments and at each step MM2 energy of the rotamer was calculated Valid low-energy rotamers were saved in a database file; those with intramol. contact or those with high-energy strain were discarded. Optimal values of dihedral angles were derived from conformational maps and applied to the modeled structure. Several families of low-energy rotamers were identified. For each family, the best representative was chosen and fully optimized with the AM1 method. The lowest-energy conformations were compared to each other and a common pharmacophore was calculated In addition, structures of ACEIs available in Cambridge **Crystallog**. Database were taken as a starting point for AM1 geometry optimization. The resulting relaxed structures were compared to those found in conformational search.

IT **87679-71-8**, Trandolaprilat **95153-31-4**, Perindoprilat
RL: PRP (Properties)
(preferred conformation of selected ACE inhibitors for interaction with ACE active site)

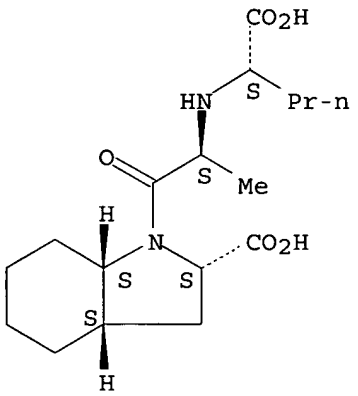
RN 87679-71-8 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-carboxy-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aR,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 95153-31-4 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-carboxybutyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L30 ANSWER 17 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:851113 HCAPLUS
DOCUMENT NUMBER: 135:371632
TITLE: Preparation of the ACE-inhibiting β-**crystalline** form of perindopril tert-butylamine salt and antihypertensive pharmaceutical formulation containing it
INVENTOR(S): Pfeiffer, Bruno; Ginot, Yves-Michel; Coquerel, Gerard; Beilles, Stephane
PATENT ASSIGNEE(S): Adir et Compagnie, Fr.
SOURCE: PCT Int. Appl., 14 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2001087836	A1	20011122	WO 2001-FR2168	20010706
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2811319	A1	20020111	FR 2000-8792	20000706
FR 2811319	B1	20020823		
CA 2415442	AA	20011122	CA 2001-2415442	20010706
EP 1294689	A1	20030326	EP 2001-954059	20010706
EP 1294689	B1	20060426		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001012244	A	20030624	BR 2001-12244	20010706
JP 2003533508	T2	20031111	JP 2001-584233	20010706
JP 3592297	B2	20041124		
EE 200300002	A	20040816	EE 2003-2	20010706
NZ 523234	A	20050128	NZ 2001-523234	20010706
US 2004029813	A1	20040212	US 2002-312902	20021231
ZA 2003000024	A	20040205	ZA 2003-24	20030102
NO 2003000050	A	20030106	NO 2003-50	20030106
BG 107533	A	20031128	BG 2003-107533	20030205
HR 2003000079	A1	20030430	HR 2003-79	20030206
JP 2005002121	A2	20050106	JP 2004-206159	20040713
US 2005203165	A1	20050915	US 2005-52489	20050204
PRIORITY APPLN. INFO.:			FR 2000-8792 A	20000706
			JP 2001-584233 A3	20010706
			WO 2001-FR2168 W	20010706
			US 2002-312902 B1	20021231

AB The more-stable β- **cryst**. form of the tert-butylamine salt of perindopril (I), characterized by its **X-ray powder diffraction** pattern, is prepared by refluxing the tert-butylamine salt of perindopril in dichloromethane, followed by cooling the mixture, and filtration. A I-contg tablet formulation is presented.

IT **107133-36-8**
RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(preparation of the ACE-inhibiting β- **cryst**. form of perindopril tert-butylamine salt and antihypertensive pharmaceutical formulation containing it)

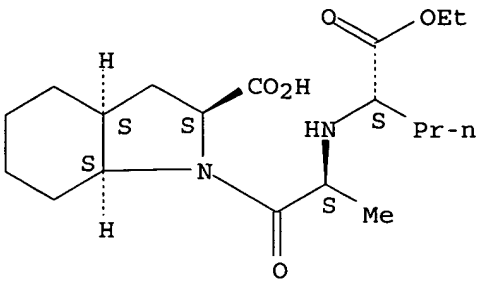
RN 107133-36-8 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

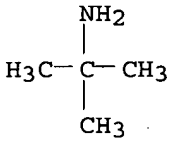
CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L30 ANSWER 18 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:851112 HCAPLUS
DOCUMENT NUMBER: 135:371631
TITLE: Preparation and **X-ray** characterization of the ACE-inhibiting α-**crystalline** form of the tert-butylamine salt of perindopril
INVENTOR(S): Pfeiffer, Bruno; Ginot, Yves-Michel; Coquerel, Gerard; Beilles, Stephane
PATENT ASSIGNEE(S): Les Laboratoires Servier, Fr.
SOURCE: PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001087835	A1	20011122	WO 2001-FR2167	20010706
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2811320	A1	20020111	FR 2000-8793	20000706

FR 2811320	B1	20020823		
CA 2415438	AA	20011122	CA 2001-2415438	20010706
EP 1296947	A1	20030402	EP 2001-954058	20010706
EP 1296947	B1	20040204		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001012367	A	20030513	BR 2001-12367	20010706
JP 2003533507	T2	20031111	JP 2001-584232	20010706
JP 3602826	B2	20041215		
AT 258918	E	20040215	AT 2001-954058	20010706
NZ 523173	A	20040430	NZ 2001-523173	20010706
PT 1296947	T	20040531	PT 2001-954058	20010706
EE 200300001	A	20040816	EE 2003-1	20010706
ES 2214434	T3	20040916	ES 2001-1954058	20010706
ZA 2002010092	A	20031212	ZA 2002-10092	20021212
US 2003186896	A1	20031002	US 2002-312961	20021231
NO 2003000024	A	20030103	NO 2003-24	20030103
BG 107532	A	20031231	BG 2003-107532	20030205
HR 2003000077	A1	20030430	HR 2003-77	20030206
US 2005059609	A1	20050317	US 2004-792355	20040303
JP 2005047902	A2	20050224	JP 2004-206158	20040713

PRIORITY APPLN. INFO.:

FR 2000-8793	A	20000706
FR 2000-8973	A	20000706
JP 2001-584232	A3	20010706
WO 2001-FR2167	W	20010706
US 2002-312961	B1	20021231

AB The α- **cryst**. form of the ACE-inhibiting tert-butylamine salt of perindopril (I) is prepared by refluxing the tert-butylamine salt of perindopril in Et acetate, cooling the mixture, and filtering the I α-**crystal** modification, which is characterized by its **powder X-ray diffraction** pattern, and a I-containing pharmaceutical formulation is prepared

IT **107133-36-8**, Perindopril erbumine
RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(preparation and **X-ray** characterization of the ACE-inhibiting α- **cryst**. form of the tert-butylamine salt of perindopril)

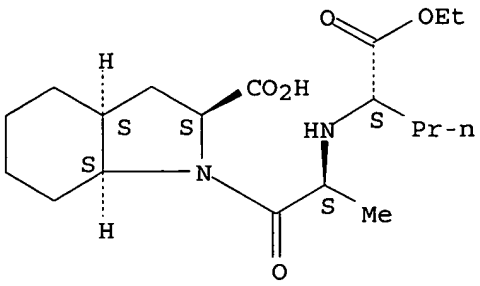
RN 107133-36-8 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

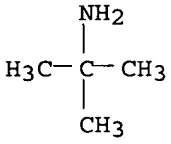
CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L30 ANSWER 19 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:816626 HCAPLUS
DOCUMENT NUMBER: 135:344373
TITLE: Process for preparing the novel γ **crystalline** form of the diuretic perindopril tert-butylamine salt
INVENTOR(S): Pfeiffer, Bruno; Ginot, Yves-Michel; Coquerel, Gerard; Beilles, Stephane
PATENT ASSIGNEE(S): Adir et Compagnie, Fr.
SOURCE: PCT Int. Appl., 11 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001083439	A2	20011108	WO 2001-FR2169	20010706
WO 2001083439	A3	20020207		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2811318	A1	20020111	FR 2000-8791	20000706

FR 2811318	B1	20020823		
CA 2415447	AA	20011108	CA 2001-2415447	20010706
AU 2001076420	A5	20011112	AU 2001-76420	20010706
EP 1296948	A2	20030402	EP 2001-954060	20010706
EP 1296948	B1	20030910		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001012211	A	20030506	BR 2001-12211	20010706
AT 249435	E	20030915	AT 2001-954060	20010706
JP 2003531890	T2	20031028	JP 2001-580868	20010706
JP 3592296	B2	20041124		
PT 1296948	T	20031231	PT 2001-954060	20010706
ES 2206423	T3	20040516	ES 2001-1954060	20010706
NZ 523311	A	20040625	NZ 2001-523311	20010706
EE 200300003	A	20040816	EE 2003-3	20010706
US 2003158121	A1	20030821	US 2002-312903	20021231
ZA 2003000025	A	20040210	ZA 2003-25	20030102
NO 2003000051	A	20030106	NO 2003-51	20030106
BG 107534	A	20031231	BG 2003-107534	20030205
HR 2003000078	A1	20030430	HR 2003-78	20030206
HR 20030078	B1	20040630		
US 2004248817	A1	20041209	US 2004-811727	20040329
JP 2005002120	A2	20050106	JP 2004-206157	20040713

PRIORITY APPLN. INFO.:

FR 2000-8791	A	20000706
JP 2001-580868	A3	20010706
WO 2001-FR2169	W	20010706
US 2002-312903	B1	20021231

AB The γ **cryst**. form of the diuretic perindopril tert-butylamine salt (I) is prepared by refluxing a chloroform-I solution, cooling the solution to 0°, and filtering the I γ **crystal** modification which is characterized by its **X-ray diffraction** pattern; a I-containing formulation is presented.

IT **107133-36-8**
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PROC (Process)
(process for preparing the novel γ **cryst**. form of the diuretic perindopril tert-butylamine salt)

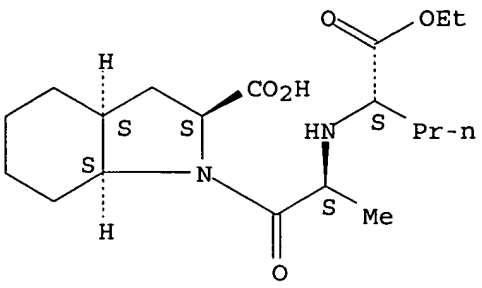
RN 107133-36-8 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

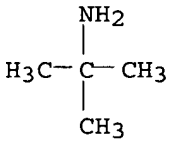
CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N



L30 ANSWER 20 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:338762 HCAPLUS
DOCUMENT NUMBER: 134:362292
TITLE: Methods of determining individual hypersensitivity to a pharmaceutical agent from gene expression profile
INVENTOR(S): Farr, Spencer
PATENT ASSIGNEE(S): Phase-1 Molecular Toxicology, USA
SOURCE: PCT Int. Appl., 222 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001032928	A2	20010510	WO 2000-US30474	20001103
WO 2001032928	A3	20020725		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-165398P P 19991105
US 2000-196571P P 20000411

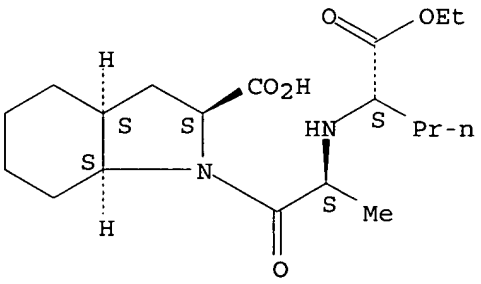
AB The invention discloses methods, gene databases, gene arrays, protein arrays, and devices that may be used to determine the hypersensitivity of individuals to a given agent, such as drug or other chemical, in order to

prevent toxic side effects. In one embodiment, methods of identifying hypersensitivity in a subject by obtaining a gene expression profile of multiple genes associated with hypersensitivity of the subject suspected to be hypersensitive, and identifying in the gene expression profile of the subject a pattern of gene expression of the genes associated with hypersensitivity are disclosed. The gene expression profile of the subject may be compared with the gene expression profile of a normal individual and a hypersensitive individual. The gene expression profile of the subject that is obtained may comprise a profile of levels of mRNA or cDNA. The gene expression profile may be obtained by using an array of nucleic acid probes for the plurality of genes associated with hypersensitivity. The expression of the genes predetd. to be associated with hypersensitivity is directly related to prevention or repair of toxic damage at the tissue, organ or system level. Gene databases arrays and apparatus useful for identifying hypersensitivity in a subject are also disclosed.

IT **82834-16-0**, Perindopril **87679-37-6**, Trandolapril
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(methods of determining individual hypersensitivity to a pharmaceutical agent
from gene expression profile)

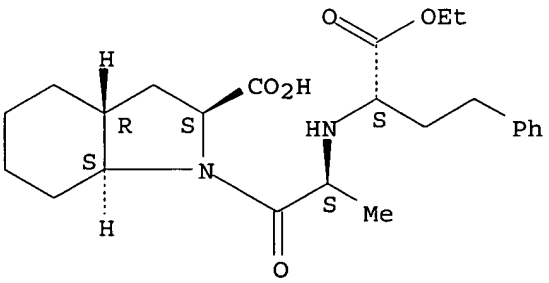
RN 82834-16-0 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 87679-37-6 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aR,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L30 ANSWER 21 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:875595 HCAPLUS
DOCUMENT NUMBER: 135:86714
TITLE: Butylaminiperindopril decreases transforming growth factor-β1 messenger RNA production in lungs of C57BL6 mice after low-dose whole-body irradiation
AUTHOR(S): Olejar, T.; Pouckova, P.; Zadinova, M.
CORPORATE SOURCE: Institute of Biophysics, Charles University, Prague, Czech Rep.
SOURCE: Drugs under Experimental and Clinical Research (2000), 26(4), 113-117
CODEN: DECRDP; ISSN: 0378-6501
PUBLISHER: Bioscience Ediprint Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Transforming growth factor (TGF)-β is believed to play a key role in the development of many autoimmune and malignant diseases, such as radiation and drug-induced organ disease. The aim of the present study was to determine mRNA production of TGF-β1 in the lungs of C57Bl6 mice after low-dose whole-body irradiation Control (irradiated) and irradiated angiotensin-converting enzyme (ACE) inhibitor-treated animals were simultaneously examined The ACE inhibitor group received butylaminiperindopril for 9 days after irradiation (7 Gy) at a daily dose of 0.1 mg/kg per rectum. On day 9, all mice were sacrificed and the production of mRNA TGF-β1 in lung tissue was determined semiquant. using reverse transcriptase polymerase chain reaction. In butylaminiperindopril-treated mice, a decrease in transcript of TGF-β1 (to 59% in comparison with controls) was observed

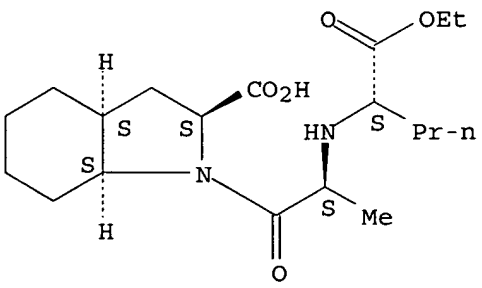
IT **107133-36-8**, Butylaminiperindopril
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(butylaminiperindopril decreases transforming growth factor-β1 mRNA production in lungs of C57BL6 mice after low-dose whole-body irradiation)

RN 107133-36-8 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

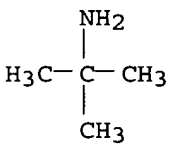
CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L30 ANSWER 22 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:480742 HCAPLUS
DOCUMENT NUMBER: 131:149349
TITLE: Drugs packaged by strip or press-through packaging and enclosed together with desiccants
INVENTOR(S): Terao, Kazuyuki; Yoshikawa, Suehiro
PATENT ASSIGNEE(S): Daiichi Seiyaku Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 4 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 11206850	A2	19990803	JP 1998-16930	19980129

PRIORITY APPLN. INFO.: JP 1998-16930 19980129

AB Solid drugs, which are packaged with a strip packaging or press-through packaging (PTP) material comprising a moisture-permeable and gas-barrier plastic sheet and an Al foil, are enclosed together with desiccant. The method prevents drugs which are instable to water, e.g. perindopril erbumine (I), etc., from deterioration due to moisture. Tablets of I were packaged with a poly(vinyl chloride) sheet ad an Al foil by PTP and enclosed in an Al-laminated plastic film bag. The bag was stored at 40° and relative humidity 75% for 6 mo. Content of I in the tablets was 96.5%.

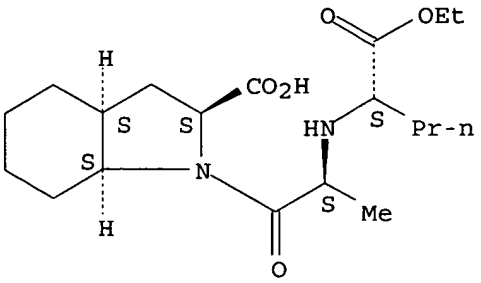
IT **107133-36-8**, Perindopril erbumine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(strip or press-through packaging of drugs with moisture-permeable and gas-barrier plastic films and Al foil and enclosing them together with desiccants)

RN 107133-36-8 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

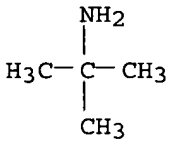
CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N



L30 ANSWER 23 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:480741 HCAPLUS
DOCUMENT NUMBER: 131:149348
TITLE: Drug desiccants and drugs stored together with the desiccants
INVENTOR(S): Terao, Kazuyuki; Yoshikawa, Suehiro
PATENT ASSIGNEE(S): Daiichi Seiyaku Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 4 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 11206849	A2	19990803	JP 1998-16929	19980129

PRIORITY APPLN. INFO.: JP 1998-16929 19980129

AB The desiccants are packed in a moisture-permeable and gas-barrier plastic bag. Solid drugs stored in a sealed container together with the desiccants are also claimed. The desiccants are useful for storing drugs instable to water and evaporable drugs. Tablets of perindopril erbumine (I) were stored in a glass bottle together with silica-alumina gel disk packed in a nylon-polyacrylonitrile laminated film at 40° and relative humidity 75% for 6 mo to show the content of I 97.3%. vs. 71.4% even after 2 mo for a control using a paper-packaged desiccant.

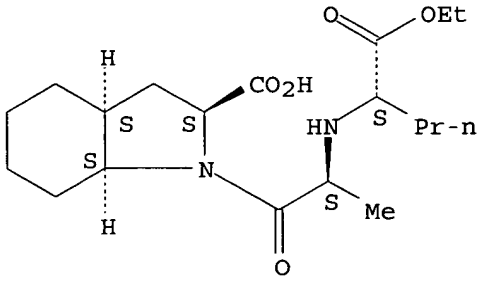
IT **107133-36-8**, Perindopril erbumine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug desiccants packed in moisture-permeable and gas-barrier plastic film bag)

RN 107133-36-8 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

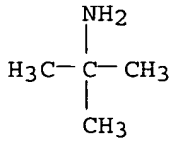
CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N



L30 ANSWER 24 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:344860 HCAPLUS
DOCUMENT NUMBER: 130:357193
TITLE: Combination of angiotensin converting enzyme inhibitor with a diuretic for treating microcirculation disorders
INVENTOR(S): Guez, David; Schiavi, Pierre; Levy, Bernard
PATENT ASSIGNEE(S): Adir et Compagnie, Fr.
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9925374	A1	19990527	WO 1998-FR411	19980303
W: AU, BR, CA, CN, HU, JP, MX, NO, NZ, PL, US, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

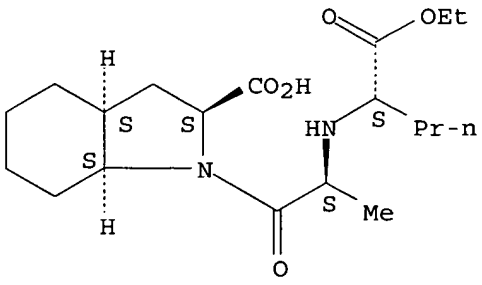
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
FR 2771010	A1	19990521	FR 1997-14485		19971119
FR 2771010	B1	20030815			
CA 2310136	AA	19990527	CA 1998-2310136		19980303
CA 2310136	C	20040420			
AU 9868377	A1	19990607	AU 1998-68377		19980303
AU 740748	B2	20011115			
EP 1032414	A1	20000906	EP 1998-913813		19980303
EP 1032414	B1	20030507			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI					
BR 9814885	A	20001003	BR 1998-14885		19980303
JP 2001523646	T2	20011127	JP 2000-520807		19980303
AT 239500	E	20030515	AT 1998-913813		19980303
NZ 504220	A	20030530	NZ 1998-504220		19980303
PT 1032414	T	20030829	PT 1998-913813		19980303
ES 2198708	T3	20040201	ES 1998-913813		19980303
ZA 9806673	A	19990204	ZA 1998-6673		19980727
NO 2000002479	A	20000512	NO 2000-2479		20000512
US 6653336	B1	20031125	US 2000-554715		20000518
PRIORITY APPLN. INFO.:			FR 1997-14485	A	19971119
			WO 1998-FR411	W	19980303

AB The use of a combination of the angiotensin converting enzyme inhibitor (IEC) with a diuretic to obtain pharmaceutical compns. for treating arteriole-capillary microcirculation disorders is disclosed. A tablet contained perindopril tert-butylamine (I) 2, indapamide (II) 0.625, colloidal silica 0.25, lactose 64.175, magnesium stearate 0.45, and **microcryst**. cellulose 22.5 mg. The efficacy of oral administration of 0.76 mg/kg/day I and 0.24 mg/kg/day II in rats is shown.

IT **82834-16-0**, Perindopril **107133-36-8**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination of angiotensin converting enzyme inhibitor with diuretic for treating microcirculation disorders)

RN 82834-16-0 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

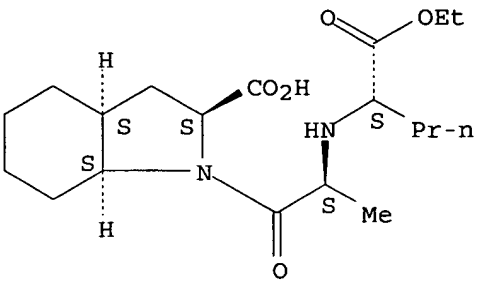


RN 107133-36-8 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

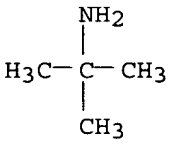
CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L30 ANSWER 25 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:7800 HCAPLUS
DOCUMENT NUMBER: 130:57229
TITLE: Controlled release pharmaceutical preparation with ACE inhibitor as active agent
INVENTOR(S): Fischer, Wilfried; Klokkers, Karin; Oppelt, Renate
PATENT ASSIGNEE(S): Hexal Ag, Germany
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9856355	A1	19981217	WO 1998-EP3536	19980612

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,

CM, GA, GN, ML, MR, NE, SN, TD, TG

DE 19724696	A1	19981224	DE 1997-19724696	19970612
CA 2295013	AA	19981217	CA 1998-2295013	19980612
AU 9883368	A1	19981230	AU 1998-83368	19980612
AU 736357	B2	20010726		
ZA 9805142	A	20000112	ZA 1998-5142	19980612
EP 994696	A1	20000426	EP 1998-933605	19980612
EP 994696	B1	20040218		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI				
TR 9903069	T2	20000522	TR 1999-9903069	19980612
NZ 501726	A	20010928	NZ 1998-501726	19980612
JP 2002504108	T2	20020205	JP 1999-501625	19980612
AT 259637	E	20040315	AT 1998-933605	19980612
ES 2216296	T3	20041016	ES 1998-933605	19980612
NO 9906049	A	20000207	NO 1999-6049	19991208
US 6267990	B1	20010731	US 1999-460055	19991213
PRIORITY APPLN. INFO.:			DE 1997-19724696 A	19970612
			WO 1998-EP3536 W	19980612

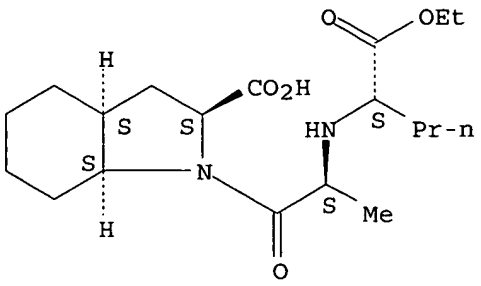
AB The title preparation contains: (i) an initial dose of active agent and optional auxiliary agents, (ii) a 1st type of controlled-release pellet in which the active agent and optional auxiliary agents are coated, and (iii) a 2nd type of controlled-release pellet in which the active agent and optional auxiliary agents are also coated. The weight ratio of the masses of the coatings in (ii) and (iii) is (1:2)-(1:7). This preparation allows an almost immediate action of the ACE inhibitor (e.g. captopril) without a marked initial peak in blood level, and maintenance of a long-lasting therapeutic blood level of the drug thereafter with very little variation. Thus, pellets A were prepared containing captopril 5, Avicel (**microcryst** . cellulose) 3, and tablettose 2 mg. Pellets A (700 g) were coated with Opadry II 40.48 and H2O 250 g, followed by a 2nd coat containing Eudragit S 100 62.5, di-Bu phthalate 6.25, 96% EtOH 350.00, and H2O 87.5 g to produce pellets B. Addnl. pellets A (700 g) were coated with Opadry II and H2O as above, followed by a coating of Eudragit S 100 192.5, di-Bu phthalate 19.25, 96% EtOH 1078, and H2O 269.5 g to produce pellets C. Pellets A 100, pellets B 700, and pellets C 700 g were dispensed into a gelatin capsule with a final captopril content of 150 mg.

IT **82834-16-0**, Perindopril **107133-36-8**, Perindopril erbumine **217460-19-0**, Perindopril hydrochloride
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(controlled release pharmaceutical preparation with ACE inhibitor as active agent)

RN 82834-16-0 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

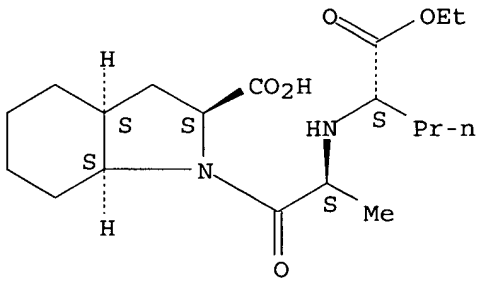


RN 107133-36-8 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

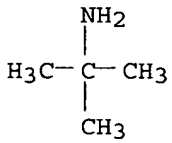
CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



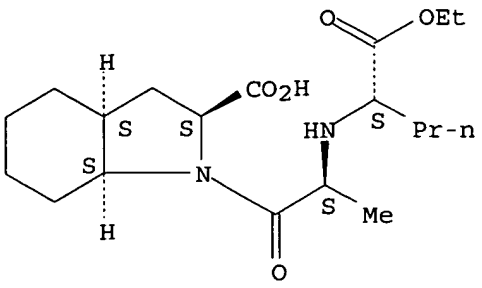
CM 2

CRN 75-64-9
CMF C4 H11 N



RN 217460-19-0 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, monohydrochloride, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



● HCl

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L30 ANSWER 26 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:64980 HCAPLUS
DOCUMENT NUMBER: 124:97758
TITLE: Drug combination containing α-lipoic acid and cardiovascular agents
INVENTOR(S): Weischer, Carl; Ulrich, Heinz; Conrad, Frank; Schmidt, Karlheinz
PATENT ASSIGNEE(S): ASTA Medica AG, Germany
SOURCE: Ger. Offen., 18 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4420102	A1	19951214	DE 1994-4420102	19940609
PRIORITY APPLN. INFO.:			DE 1994-4420102	19940609

AB A synergistic combination for treatment of cardiovascular and diabetes-associated disorders contains α-lipoic acid (or its enantiomers, derivs., or metabolites), ≥1 organic nitrate, Ca2+ antagonist, angiotensin-converting enzyme inhibitor, or oxyfedrine. Thus, 400-mg tablets were prepared from a mixture containing (S)-α-lipoic acid 250, oxyfedrine 40, **microcryst**. cellulose 760, starch 250, lactose 682.5, Mg stearate 15, and highly disperse SiO2 2.5 g.

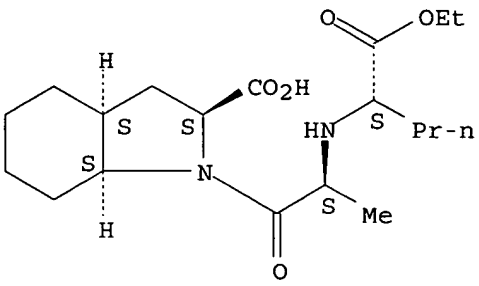
IT **107133-36-8**, Perindopril-tert-butylamine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug combination containing α-lipoic acid and cardiovascular agents)

RN 107133-36-8 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

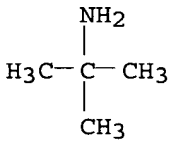
CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N



L30 ANSWER 27 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:620945 HCAPLUS
DOCUMENT NUMBER: 121:220945
TITLE: Pharmacokinetics of perindopril erbumine in rats. 2. Blood level profile, distribution, metabolism and excretion after repeated oral administration
AUTHOR(S): Nakaoka, Minoru; Hakusui, Hideo; Jin, Yoshitaka; Tutumi, Syuichirou; Hironaka, Akiko; Hirano, Hiromi; Noguchi, Tomoyuki; Uohama, Katsumi; Takasaki, Michika; et al.
CORPORATE SOURCE: Developmental Research Laboratories, Daiichi Pharmaceutical Co., Ltd., Tokyo, Japan
SOURCE: Yakubutsu Dotai (1994), 9(2), 247-57
CODEN: YADOEL; ISSN: 0916-1139
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

AB Pharmacokinetic studies on blood level, tissue distribution, metabolism and excretion of [14C]perindopril erbumine, an angiotensin-converting enzyme (ACE) inhibitor, were performed in rats during and after repeated oral administration of at 0.5 mg/kg/day for 14 days. The blood levels of radioactivity reached a steady state after 5 days, and the equivalent concentration on day 5 was 7.09 ng/mL. After repeated oral administration, the radioactivity was mainly distributed in the lungs, kidneys, liver and intestinal tract. The radioactivity was highest in the lungs, which contain high ACE activity, and reached a steady state after 14 days. Elimination of radioactivity from most of tissues was rapid. It is assumed that the accumulation of radioactivity in the plexus choroideus arose from high localization of ACE. The excretion rate in the urine and

feces during repeated oral administration was almost constant At 168 h after the last dose, the extent of excretion of radioactivity was 33.1% and 69.6% of the total dose in the urine and feces, resp. An active metabolite, perindoprilat, was found, which accounted for most of the radioactivity in the plasma, lungs, liver and kidneys, and also in the urine and feces.

IT **107133-36-8**, Perindopril erbumine
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(perindopril erbumine pharmacokinetics and metabolism)

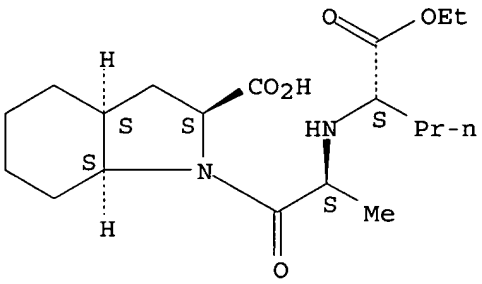
RN 107133-36-8 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

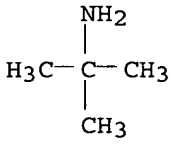
CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N



L30 ANSWER 28 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:620944 HCAPLUS
DOCUMENT NUMBER: 121:220944
TITLE: Pharmacokinetics of perindopril erbumine in rats. 1. Plasma level profile, distribution, metabolism and excretion after single oral administration
AUTHOR(S): Suzuki, Wataru; Kato, Kinuyo; Nakaoka, Minoru; Hakusui, Hideo; Jin, Yoshitaka; Katami, Yoshiharu; Nogami, Takahiro; Shiina, Michiko; Otsu, Yuko; et al.
CORPORATE SOURCE: Developmental Research Laboratories, Daiichi

Pharmaceutical Co., Ltd., Tokyo, Japan
SOURCE: Yakubutsu Dotai (1994), 9(2), 235-46
CODEN: YADOEL; ISSN: 0916-1139
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

AB Pharmacokinetic studies on plasma level, tissue distribution, metabolism and excretion of [14C]perindopril erbumine, an angiotensin-converting enzyme (ACE) inhibitor, were performed in fasting male rats after single oral administration at 0.5 mg/kg. The radioactivity in plasma reached a maximum equivalent to 88 ng/mL after 1 h, and the elimination half-lives were 2.1 h (2-8 h) and 34 h (24-72 h). After single oral administration, the radioactivity was rapidly distributed to tissues, reaching maximum levels after 1 h in most tissues. After 8 h, a high level of radioactivity was detected in the lungs, pituitary gland, intestines, kidneys and aorta, due to high localization of ACE in these tissues. After 168 h, the level of radioactivity was reduced in all tissues. After 168 h, the radioactivity excreted in the urine and feces accounted for 39.7% and 58.7% of the dose, resp. Biliary excretion of radioactivity was 31.2% within 48 h. The total recoveries from urine, bile and carcass accounted for 75.4% of the dose, suggesting good gastrointestinal absorption. An active metabolite, perindoprilat, was found, which accounted for most of the radioactivity in the plasma, lungs, liver and kidneys, and also in the urine and feces. A linear dose dependency of the pharmacokinetics was observed

IT **107133-36-8**, Perindopril erbumine
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(perindopril erbumine pharmacokinetics and metabolism)

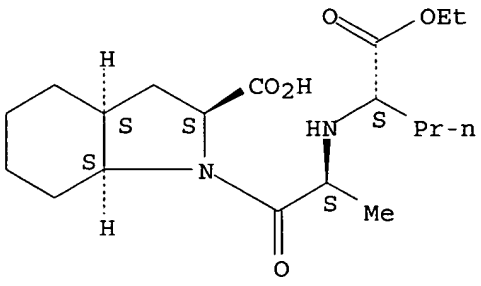
RN 107133-36-8 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

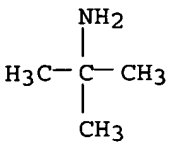
CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

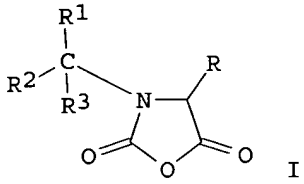
CRN 75-64-9
CMF C4 H11 N



L30 ANSWER 29 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1991:207829 HCAPLUS
DOCUMENT NUMBER: 114:207829
TITLE: Preparation of carboxyalkyl dipeptides useful as angiotensin-converting enzyme (ACE) inhibitors
INVENTOR(S): Oudenes, Jan; Schleicher, Richard Henry
PATENT ASSIGNEE(S): Pharma Investi S. A., Spain
SOURCE: Span., 10 pp.
CODEN: SPXXAD
DOCUMENT TYPE: Patent
LANGUAGE: Spanish
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ES 2004804	A6	19890201	ES 1987-2390	19870813
PRIORITY APPLN. INFO.:			ES 1987-2390	19870813

OTHER SOURCE(S): MARPAT 114:207829
GI



I

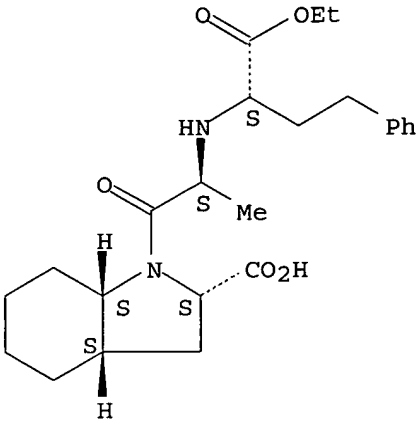
AB R1R2R3CNHCHRCONR4CHR5COR6 [R, R1, R2 = H, alkyl, Ph, phenylalkyl, alkylphenyl, aminoalkyl, protected aminoalkyl; R3 = CO2H or its ester; R4 = H, alkyl; R5 = H, alkyl, Ph, phenylalkyl, alkylphenyl; R4R5 may form (un)substituted C4-9 monocyclic or fused bicyclic nucleus; R6 = OH, alkoxy, alkenyloxy, OPh, alkylsilyloxy, etc.], including such ACE inhibitors as enalapril, lisinopril, indolapril, ramipril, and quinapril, were prepared by converting carboxylakyl R1R2R3CNHCHRCO2H to cyclic anhydrides I, reaction of I with R4NHCHR5COR6, and optional deprotection, saponification of R6, or salification. Thus, N-(1-S-ethoxycarbonyl-3-phenylpropyl)-L-alanine was treated with 1,1-carbonyldiimidazole in EtOAc at 20°, followed by L-proline. Two **crystns**. with maleic acid gave first imidazole maleate byproduct and then 77% 1-[N-[(S)-1-(ethoxycarbonyl)-3-phenylpropyl]-L-alanyl]-L-proline, i.e. enalapril maleate.

IT **80876-01-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, via cyclic anhydride)

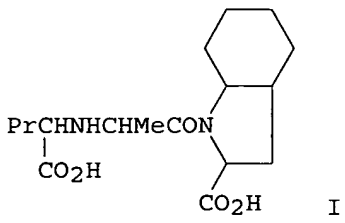
RN 80876-01-3 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)-3-

phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L30 ANSWER 30 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1991:74706 HCAPLUS
DOCUMENT NUMBER: 114:74706
TITLE: Configuration and preferential solid-state conformations of perindoprilat (S-9780). Comparison with the crystal structures of other ACE inhibitors and conclusions related to structure-activity relationships
AUTHOR(S): Pascard, Claudine; Guilhem, Jean; Vincent, Michel; Remond, Georges; Portevin, Bernard; Laubie, Michel
CORPORATE SOURCE: Inst. Chim. Subst. Nat., Gif-sur-Yvette, 91198, Fr.
SOURCE: Journal of Medicinal Chemistry (1991), 34(2), 663-9
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



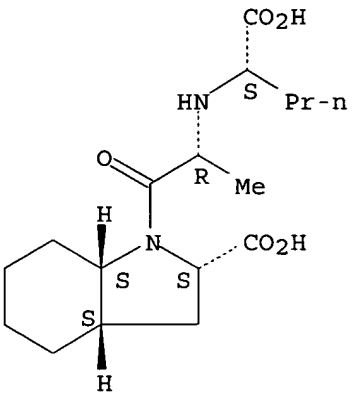
I

AB The conformational of perindoprilat (I), an antihypertensive drug, is studied in the solid state by **X-ray** anal. The resolution of its structure reveals important analogies between its observed conformation and that of several angiotensin-converting enzyme (ACE) inhibitors of the same family. This comparison points out a constant relative orientation of the functional groups, regardless of the mol. environment. This angular constancy appears not to be accidental and is a

good argument for the spatial design of the ACE binding site. Although ACE is a carboxydipeptidase, the binding site may not contain two but one unique hydrophobic pocket receiving the C-terminal end of the inhibitors.

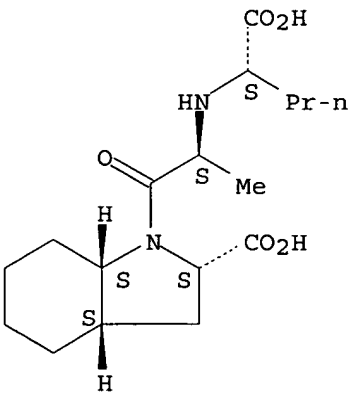
IT **130982-51-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and angiotensin-converting enzyme inhibition by, perindoprilat in relation to)
RN 130982-51-3 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[(1-carboxybutyl)amino]-1-oxopropyl]octahydro-, [2S-[1[S*(R*)],2α,3aβ,7aβ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **95153-31-4P**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation and crystal structure of, angiotensin-converting enzyme inhibition and antihypertensive activity in relation to)
RN 95153-31-4 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-carboxybutyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

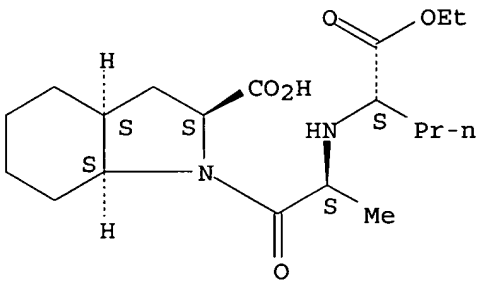
Absolute stereochemistry.



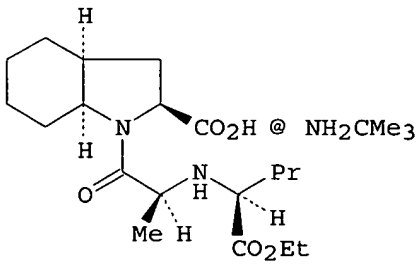
IT **82834-16-0**, Perindopril
RL: RCT (Reactant); RACT (Reactant or reagent)
(saponification of)

RN 82834-16-0 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

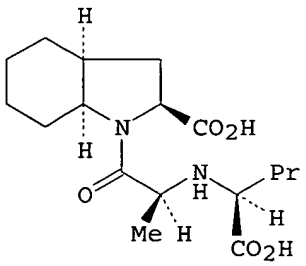
Absolute stereochemistry. Rotation (-).



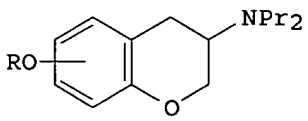
L30 ANSWER 31 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1990:118595 HCAPLUS
DOCUMENT NUMBER: 112:118595
TITLE: Some syntheses of tritium biochemicals at high specific radioactivity: radiosyntheses of ACE inhibitors, 5-HT1A and dopamine receptors radioligands
AUTHOR(S): Pichat, L.
CORPORATE SOURCE: CEA - CEN Saclay, Gif-sur-Yvette, 91191, Fr.
SOURCE: Synth. Appl. Isot. Labelled Cpd. 1988, Proc. Int. Symp. (1989), Meeting Date 1988, 21-6. Editor(s): Baillie, Thomas A.; Jones, John Richards. Elsevier: Amsterdam, Neth.
CODEN: 56OXA8
DOCUMENT TYPE: Conference
LANGUAGE: English
GI



I



II



III

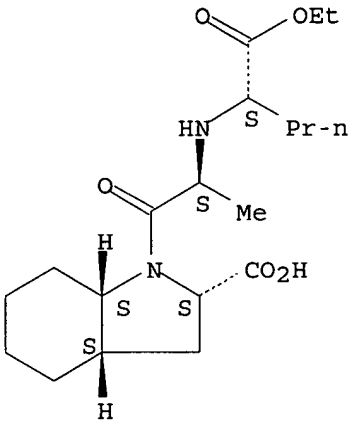
AB A lecture with 9 refs. Synthesis of tritium labeled biochems. I and II as potent inhibitors of angiotensin converting enzyme (ACE) and III (OR = 5-OMe, 8-OMe) as D2 receptors is described.

IT **125650-71-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as angiotensin converting enzyme inhibitors)
RN 125650-71-7 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, labeled with tritium, [2S-[1[R*(R*)],2α,3aβ,7aβ]]-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

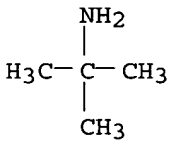
CRN 125650-70-6
CMF C19 H32 N2 O5
CIL XH-13

Absolute stereochemistry.



CM 2

CRN 75-64-9
CMF C4 H11 N

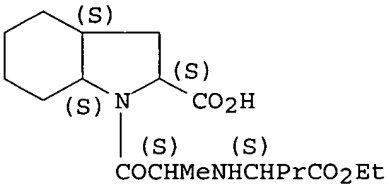


L30 ANSWER 32 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1989:515749 HCAPLUS
DOCUMENT NUMBER: 111:115749
TITLE: Preparation of perindopril via acylation of perhydroindolecarboxylate with N-[(ethoxycarbonyl)butyl]alanine
INVENTOR(S): Vincent, Michel; Baliarda, Jean; Marchand, Bernard; Remond, Georges
PATENT ASSIGNEE(S): ADIR, Fr.
SOURCE: Eur. Pat. Appl., 25 pp.

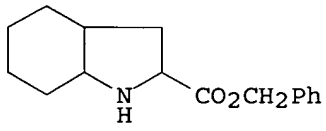
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
EP 308341	A1	19890322	EP 1988-402339		19880916
EP 308341	B1	19901212			
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE					
FR 2620709	A1	19890324	FR 1987-12896		19870917
FR 2620709	B1	19900907			
CA 1336348	A1	19950718	CA 1988-577078		19880907
DK 8805151	A	19890318	DK 1988-5151		19880915
DK 171470	B1	19961111			
AU 8822362	A1	19890323	AU 1988-22362		19880916
AU 608363	B2	19910328			
JP 01110696	A2	19890427	JP 1988-232125		19880916
JP 05043717	B4	19930702			
ZA 8806932	A	19890530	ZA 1988-6932		19880916
US 4914214	A	19900403	US 1988-245446		19880916
AT 59047	E	19901215	AT 1988-402339		19880916
CA 1338015	A1	19960130	CA 1991-616239		19911128
PRIORITY APPLN. INFO.:			FR 1987-12896	A	19870917
			CA 1988-577078	A3	19880907
			EP 1988-402339	A	19880916

OTHER SOURCE(S): MARPAT 111:115749
GI



I



II

AB Preparation of perindopril via acylation of perhydroindolecarboxylate with N-[(ethoxycarbonyl)butyl]alanine. The title compound (I), useful as an antihypertensive (no data), is prepared, e.g., via N-acylation of perhydroindole derivative II (preparation given) with (S,S)-HO2CCHMeNHCHPrCO2Et (III). II.p-MeC6H4SO3H (preparation given) was condensed with III in EtOAc containing Et3N, 1-hydroxybenzotriazole, and dicyclohexylcarbodiimide to give, after deprotection and treatment with Me3CNH2, I.Me3CNH2.

IT **107133-36-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, via acylation of perhydroindole derivative with N-[(ethoxycarbonyl)butyl]alanine)

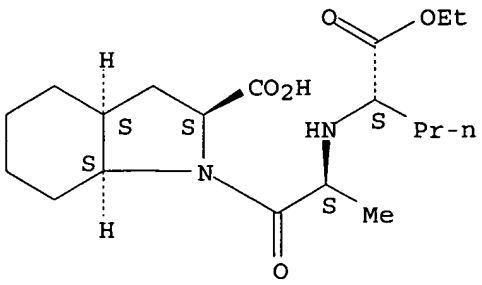
RN 107133-36-8 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

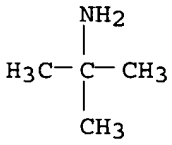
CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N



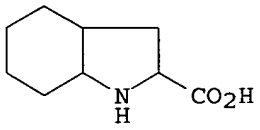
L30 ANSWER 33 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1989:477846 HCAPLUS
DOCUMENT NUMBER: 111:77846
TITLE: Industrial preparation of (2S,3aS,7aS)-perhydroindole-2-carboxylic acid as intermediate for antihypertensive perindopril
INVENTOR(S): Vincent, Michel; Baliarda, Jean; Marchand, Bernard; Remond, Georges
PATENT ASSIGNEE(S): ADIR, Fr.
SOURCE: Eur. Pat. Appl., 16 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 308339	A1	19890322	EP 1988-402337	19880916
EP 308339	B1	19920506		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
FR 2620703	A1	19890324	FR 1987-12900	19870917
FR 2620703	B1	19911004		
DK 8805149	A	19890318	DK 1988-5149	19880915
AU 8822361	A1	19890323	AU 1988-22361	19880916
AU 618752	B2	19920109		
ZA 8806931	A	19890530	ZA 1988-6931	19880916

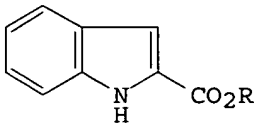
US 4935525	A	19900619	US 1988-245352		19880916
JP 02191251	A2	19900727	JP 1988-232123		19880916
AT 75735	E	19920515	AT 1988-402337		19880916
ES 2033450	T3	19930316	ES 1988-402337		19880916
US 4954640	A	19900904	US 1990-462797		19900110
PRIORITY APPLN. INFO.:			FR 1987-12900	A	19870917
			EP 1988-402337	A	19880916
			US 1988-245352	A3	19880916

OTHER SOURCE(S): CASREACT 111:77846; MARPAT 111:77846

GI



I



II

AB The title compound (I), useful as an intermediate for antihypertensive perindopril, was prepared from indolecarboxylic acid derivs. II (R = H, lower alkyl). Esterification of II (R = H) in EtOH containing H2SO4, reduction with Sn in EtOH containing HCl, saponification, and resolution gave (S)-indoline-2-carboxylic acid (III). Hydrogenation of III over Rh under H2 at 60° gave (2S,3aS,7aS)-octahydroindole-2-carboxylic acid.

IT **107133-36-8**
RL: RCT (Reactant); RACT (Reactant or reagent)
(intermediate for, octahydroindolecarboxylic acid as)

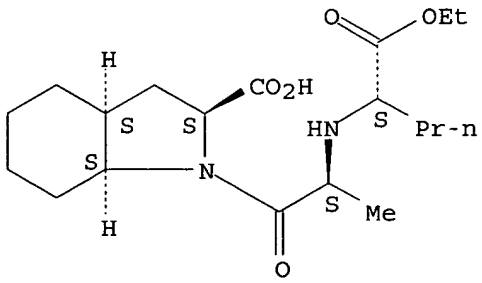
RN 107133-36-8 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

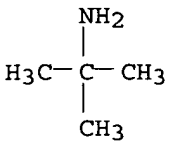
CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

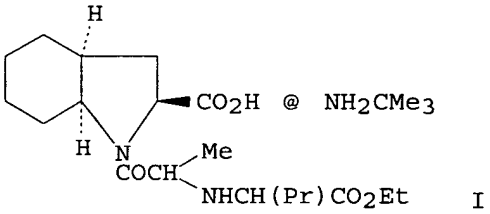


CM 2

CRN 75-64-9
CMF C4 H11 N



L30 ANSWER 34 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1989:204950 HCAPLUS
DOCUMENT NUMBER: 110:204950
TITLE: Gas chromatography-mass spectrometry of perindopril and its active free metabolite, an angiotensin convertase inhibitor: choice of derivatives and ionization modes
AUTHOR(S): Tsaconas, Christos; Devissaguet, Michele; Padieu, Prudent
CORPORATE SOURCE: Cent. Spectrom. Masse, Fac. Med., Dijon, F-21033, Fr.
SOURCE: Journal of Chromatography (1989), 488(1), 249-65
CODEN: JOCRAM; ISSN: 0021-9673
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB Perindopril (I), a perhydroindole compound and a novel class of angiotensin convertase inhibitor, after oral administration leads to an active metabolite by de-esterification of the Et ester. Routine biol. measurements are currently done using a radioimmunol. assay, but a mass fragmento-graphic method was developed using plasma spiked with the drugs, which were then derivatized to the iso-Bu ester heptofluorobutyramide and assayed using ammonia neg. chemical ionization. Levels of 100 pg/mL were assayed. However, isobutanol derivatization provoked partial transesterification of the Et ester of the parent drug into the diisobutyl ester derivative, which corresponds to the active metabolite. A second method of derivatization to stable trimethylsilyl esters preserved the original Et ester of the parent drug. Despite the lower ionization yields, the mass fragmentog. method was sensitive and accurate enough to work satisfactorily at the 2 ng/mL level in spiked plasma, which is the level found currently in patients.

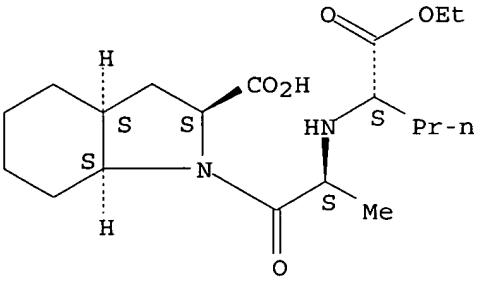
IT **107133-36-8**, S-9490-3
RL: ANT (Analyte); ANST (Analytical study)
(determination of, in blood plasma of humans by gas chromatog.-mass spectrometry, derivatization and ionization modes for)

RN 107133-36-8 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

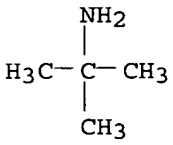
CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



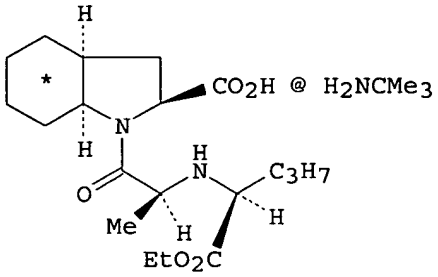
CM 2

CRN 75-64-9
CMF C4 H11 N

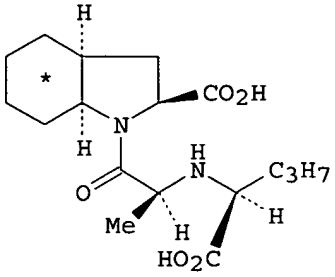


L30 ANSWER 35 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1988:631529 HCAPLUS
DOCUMENT NUMBER: 109:231529
TITLE: Synthesis of S9490-3 [U-14C-cyclohexyl] 1-[(2S)2-[(1S)1-(ethoxycarbonylbutyl)amino]-1-oxopropyl]-(2S,3aS,7aS)-perhydroindole-2-carboxylic acid tert-butylamine salt and S9780 [U-14C-cyclohexyl] 1-[(2S)2-[(1S)1-(carboxybutyl)amino]-1-oxopropyl]-2S,3aS,7aS)-perhydroindole-2-carboxylic acid and of [3,4-3H-butylamino]S9490-3 and [(3,4-3H-)butylamino]S9780
AUTHOR(S): Pichat, L.; Tostain, J.; Gomis, J. M.; Coppo, M.; Moustier, A. M.; Vincent, M.; Remond, G.; Portevin, B.; Laubie, M.
CORPORATE SOURCE: CEN Saclay, Gif sur Yvette, 91191, Fr.
SOURCE: Journal of Labelled Compounds and Radiopharmaceuticals (1988), 25(5), 553-68
CODEN: JLCRD4; ISSN: 0362-4803
DOCUMENT TYPE: Journal
LANGUAGE: French

OTHER SOURCE(S): CASREACT 109:231529
GI



I



II

AB The title 14C-labeled compds. I (* signifies the uniform labeling of the cyclohexane ring with 14C) and II were prepared from aniline-U-14C in several steps. The title 3H-labeled compds. were also prepared The latter synthesis involved the tritiation of an allylglycine residue. The title compds. are potent inhibitors of angiotensin-converting enzyme.

IT **117770-49-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and saponification of)

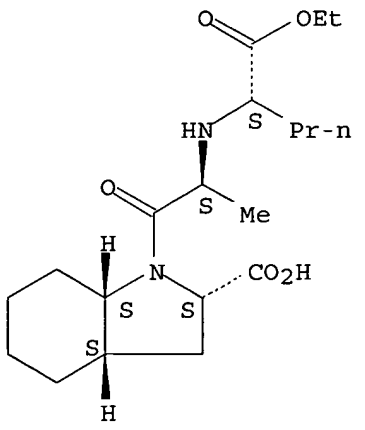
RN 117770-49-7 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, labeled with carbon-14, [2S-[1[R*(R*)],2α,3aα,7aβ]]-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

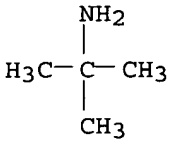
CRN 117770-48-6
CMF C19 H32 N2 O5
CIL XC-14

Absolute stereochemistry.



CM 2

CRN 75-64-9
CMF C4 H11 N

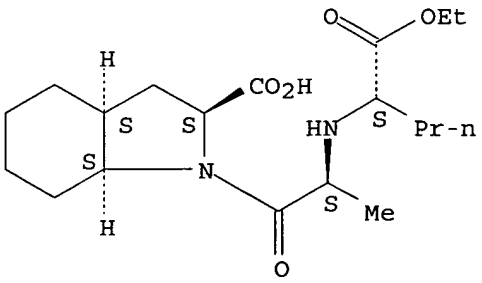


L30 ANSWER 36 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1988:87332 HCAPLUS
DOCUMENT NUMBER: 108:87332
TITLE: New convertase inhibitors
AUTHOR(S): Wiecek, Andrzej; Grzeszczak, Wladyslaw
CORPORATE SOURCE: Klin. Nefrol., Slaska Akad. Med., Katowice, 40-027, Pol.
SOURCE: Polskie Archiwum Medycyny Wewnetrznej (1986), 76(5-6 /11-12/), 291-7
CODEN: PAMWAL; ISSN: 0032-3772
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Polish
AB A review, with 27 refs., of inhibitors of angiotensin-converting enzyme, including MK 521, ramipril (Hoe 498), perindopril (S-9490-3), pivalopril (RHC 3659(S)), CI 906, CI 607, CGS 13945, CGS 13934, CGS 14824A, and L 681176.
IT **107133-36-8**, S-9490-3
RL: BIOL (Biological study)
(angiotensin-converting enzyme inhibition by)
RN 107133-36-8 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

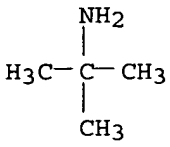
CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

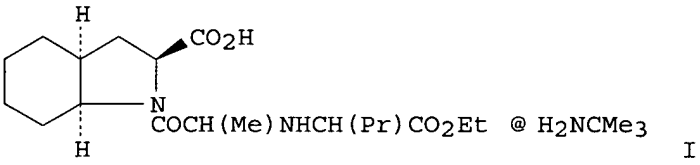


CM 2

CRN 75-64-9
CMF C4 H11 N



L30 ANSWER 37 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1987:113304 HCAPLUS
DOCUMENT NUMBER: 106:113304
TITLE: Perindopril, converting enzyme blockade, and peripheral arterial hemodynamics in the healthy volunteer
AUTHOR(S): Richer, C.; Thuillez, C.; Giudicelli, J. F.
CORPORATE SOURCE: Serv. Pharmacol. Clin., Hop. Bicetre, Le Kremlin-Bicetre, 94275, Fr.
SOURCE: Journal of Cardiovascular Pharmacology (1987), 9(1), 94-102
CODEN: JCPCDT; ISSN: 0160-2446
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

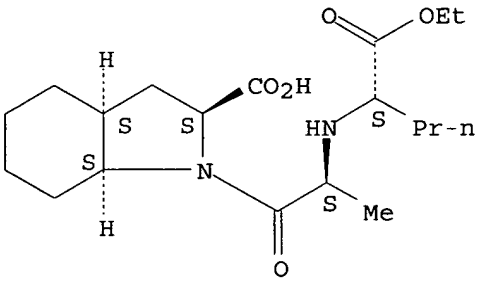
AB The effects of three doses (4, 8, and 16 mg) of perindopril tert-butylamine salt (I) [**107133-36-8**], a new angiotensin I converting enzyme [9015-82-1] inhibitor, on systemic blood pressure, heart rate, brachial and carotid artery flow and diameter (assessed by the pulsed Doppler technique), forearm vascular resistance, plasma converting enzyme and renin [9015-94-5] activities, and plasma aldosterone [52-39-1] were investigated in the normal volunteer and compared with those of a placebo over a 24-h period following oral drug intake in a double-blind, cross-over trial. I dose-dependently decreased plasma converting enzyme activity, an effect that peaked at 3-4 h and persisted up to at least 48 h. Plasma renin activity increased for 12 h and plasma aldosterone was slightly decreased. Systemic blood pressure and heart rate were not drug-affected but I dose-dependently augmented brachial and carotid artery flow, indicating an increase in peripheral arterial compliance. These vasodilating effects, which lasted up to 10 h after drug intake, affected both large arteries and arterioles, the latter being more sensitive, however, and were more marked in the muscular resistance vessels.
IT **107133-36-8**

RL: PRP (Properties)
(converting enzyme inhibition and cardiovascular effects of, in humans)
RN 107133-36-8 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

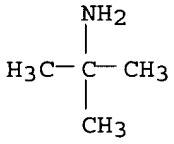
CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N



L30 ANSWER 38 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1985:25038 HCAPLUS
DOCUMENT NUMBER: 102:25038
TITLE: Carboxyalkyl dipeptides
INVENTOR(S): Geiger, Rolf; Teetz, Volker; Urbach, Hansjoerg; Henning, Rainer
PATENT ASSIGNEE(S): Hoechst A.-G. , Fed. Rep. Ger.
SOURCE: Ger. Offen., 24 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3303139	A1	19840809	DE 1983-3303139	19830131
HU 34159	O	19850228	HU 1984-312	19840125

HU 191120	B	19870128		
FI 8400350	A	19840801	FI 1984-350	19840127
FI 88153	B	19921231		
FI 88153	C	19930413		
EP 115345	A1	19840808	EP 1984-100858	19840127
EP 115345	B1	19880107		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
AT 31720	E	19880115	AT 1984-100858	19840127
DK 8400415	A	19840801	DK 1984-415	19840130
DK 174386	B1	20030127		
NO 8400350	A	19840801	NO 1984-350	19840130
NO 166641	B	19910513		
NO 166641	C	19910821		
JP 59141545	A2	19840814	JP 1984-13540	19840130
JP 05047538	B4	19930719		
ES 529272	A1	19841001	ES 1984-529272	19840130
IL 70830	A1	19880229	IL 1984-70830	19840130
CA 1283249	A1	19910416	CA 1984-446349	19840130
AU 8423933	A1	19840802	AU 1984-23933	19840131
AU 566589	B2	19871022		
ES 531284	A1	19841201	ES 1984-531284	19840404
FI 8802285	A	19880516	FI 1988-2285	19880516
CA 1317067	A2	19930427	CA 1988-576609	19880906
NO 9003546	A	19840801	NO 1990-3546	19900813
NO 171976	B	19930215		
NO 171976	C	19930526		
JP 05017439	A2	19930126	JP 1991-27801	19910130
JP 07088358	B4	19950927		

PRIORITY APPLN. INFO.:	DE 1983-3303112	A	19830131
	DE 1983-3303139	A	19830131
	EP 1984-100858	A	19840127
	FI 1984-350	A	19840127
	CA 1984-446349	A3	19840130
	NO 1984-350	A1	19840130

OTHER SOURCE(S): CASREACT 102:25038

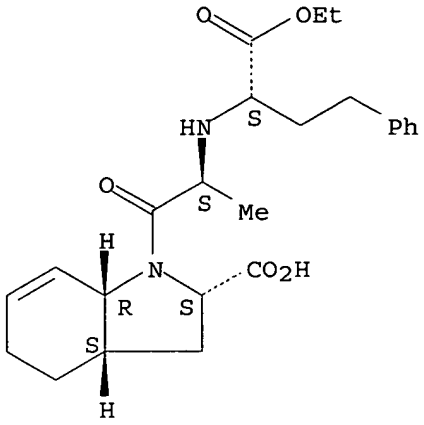
GI For diagram(s), see printed CA Issue.

AB Title compds. I [R = R1 = H, R2R3 = (CH2)n (n = 3, 4, 5, 6) or (CH2)pCH:CH(CH2)q (p + q = 1, 2, 3, 4); RR1 = (CH2)n (n = 3, 5, 6) or (CH2)pCH:CH(CH2)q (p + q = 1, 2, 3, 4), R2 = R3 = H; R = R3 = H, R1R2 = (CH2)r (r = 4, 5, 6, 7); R4 = CO2H, R5 = H; R4 = H, R5 = CO2H; R6 = H, (un)substituted C1-6 aliphatic residue, (un)substituted C6-12 aromatic residue, etc.; R7 = H, (un)substituted C1-6 aliphatic residue, substituted C7-15 araliph. residue; R8 = H, OH; R9 = H, R8R9 = O; R10 = C1-6 aliphatic residue, C5-9 cycloaliph. residue, (un)substituted C6-12 aromatic residue, indolyl; m = 0, 1] were prepared by condensation of proline analogs II [R4 = CO2R11, R5 = H; R4 = H, R5 = CO2R11; R11 = (un)substituted C1-6 aliphatic residue, (un)substituted C6-12 aromatic residue, etc.] with HO2CCHR6NHCH(CO2R7)(CH2)mCR8R9R10, followed by cleaving R11 by hydrogenolysis or hydrolysis. Thus, alanine derivative III was refluxed in 2N HCl for 45 min and then hydrogenated over Pd/C to give the cis-endo isomer of azabicyclo[3.3.0]octanecarboxylate IV.HCl (R12 = H), which was esterified with PhCH2OH/SOCl2 to give racemic IV·HCl (R12 = CH2Ph) (V). The latter was resolved by **crystn**. of its PhCH2O2C-L-Phe-OH salt to give (1S, 3S, 5S)-V, which was condensed with (S)-PhCH2CH2CH(CO2Et)-L-Ala-OH by DCC to give dipeptide cis-endo-(3S)-VI (R12 = CH2Ph), which was debenzylated by hydrogenolysis over Pd/C to give cis-endo-(3S)-VI (R12 = H). I are antihypertensives (no data) due to their ability to inhibit angiotensin-converting enzyme.

IT **89162-81-2P**

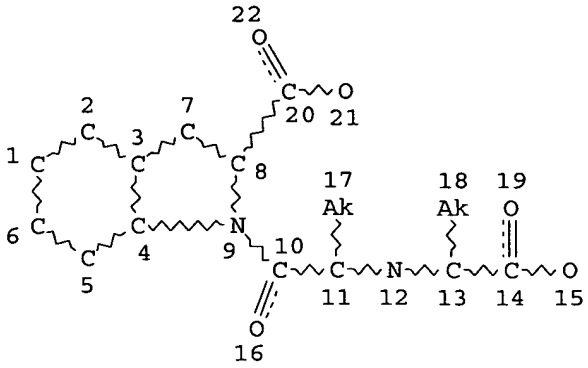
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 89162-81-2 HCAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-2,3,3a,4,5,7a-hexahydro-, monohydrochloride, [2S-[1[R*(R*)],2α,3aβ,7aβ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

=> d que l15
L1 421 SEA FILE=HCAPLUS ABB=ON PLU=ON ("PFEIFFER B"/AU OR "PFEIFFER B VICTOR"/AU) OR "PFEIFFER BRUNO"/AU
L2 13 SEA FILE=HCAPLUS ABB=ON PLU=ON ("GINOT Y M"/AU OR "GINOT Y MICHEL"/AU OR "GINOT YVES MICHEL"/AU)
L3 85 SEA FILE=HCAPLUS ABB=ON PLU=ON ("COQUEREL G"/AU OR "COQUEREL GERARD"/AU)
L4 6 SEA FILE=HCAPLUS ABB=ON PLU=ON ("BEILLES S"/AU OR "BEILLES STEPHANE"/AU)
L5 513 SEA FILE=HCAPLUS ABB=ON PLU=ON (L1 OR L2 OR L3 OR L4)
L6 3 SEA FILE=HCAPLUS ABB=ON PLU=ON L5 AND ?PERINDOPR?
L7 6 SEA FILE=HCAPLUS ABB=ON PLU=ON (L1 AND (L2 OR L3 OR L4)) OR (L2 AND (L3 OR L4)) OR (L3 AND L4)
L8 6 SEA FILE=HCAPLUS ABB=ON PLU=ON (L6 OR L7)
L9 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 22

STEREO ATTRIBUTES: NONE
L11 710 SEA FILE=REGISTRY SSS FUL L9
L12 1473 SEA FILE=HCAPLUS ABB=ON PLU=ON L11
L14 3 SEA FILE=HCAPLUS ABB=ON PLU=ON L12 AND L5
L15 6 SEA FILE=HCAPLUS ABB=ON PLU=ON L8 OR L14

=> d l15 ibib abs 1-6

L15 ANSWER 1 OF 6 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:934234 HCAPLUS
DOCUMENT NUMBER: 136:191893
TITLE: Oscillating Crystallization in Solution between (+)- and (-)-5-Ethyl-5-methylhydantoin under the Influence of Stirring
AUTHOR(S): Gervais, Claire; **Beilles, Stephane**; Cardinaeel, Pascal; Petit, Samuel; **Coquerel, Gerard**
CORPORATE SOURCE: Unite de Croissance Cristalline et de Modelisation Moleculaire (UC2M2), UPRES EA 2659 IRCOF, Universite de Rouen, Mont Saint-Aignan, F-76821, Fr.
SOURCE: Journal of Physical Chemistry B (2002), 106(3), 646-652
CODEN: JPCBFK; ISSN: 1089-5647
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Although the title compound crystallizes as a stable conglomerate without any detectable solid solution, particles in the shape of single crystals grown from the racemic aqueous solution without stirring contain almost no enantiomeric excess. From stereoselective dissoln. expts. carried out in a solution saturated with a single enantiomer, the formation of these particles results from the epitaxial association of macroscopic homochiral lamellar fragments parallel to the {101} faces. This alternated 2-dimensional nucleation and growth process is shown to constitute an oscillating crystallization mechanism controlled by diffusion only. This is confirmed by the

implementation of a gentle stirring of the mother liquor during the crystallization which led to crystals having a high enantiomeric excess. Mol. modeling studies indicate that the epitaxial region can be described at a mol. level. The structure of two racemic compds. could be generated from this epitaxial zone.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:851113 HCAPLUS
DOCUMENT NUMBER: 135:371632
TITLE: Preparation of the ACE-inhibiting β-crystalline form of **perindopril** tert-butylamine salt and antihypertensive pharmaceutical formulation containing it
INVENTOR(S): **Pfeiffer, Bruno; Ginot, Yves-Michel ; Coquerel, Gerard; Beilles, Stephane**
PATENT ASSIGNEE(S): Adir et Compagnie, Fr.
SOURCE: PCT Int. Appl., 14 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001087836	A1	20011122	WO 2001-FR2168	20010706
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2811319	A1	20020111	FR 2000-8792	20000706
FR 2811319	B1	20020823		
CA 2415442	AA	20011122	CA 2001-2415442	20010706
EP 1294689	A1	20030326	EP 2001-954059	20010706
EP 1294689	B1	20060426		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001012244	A	20030624	BR 2001-12244	20010706
JP 2003533508	T2	20031111	JP 2001-584233	20010706
JP 3592297	B2	20041124		
EE 200300002	A	20040816	EE 2003-2	20010706
NZ 523234	A	20050128	NZ 2001-523234	20010706
US 2004029813	A1	20040212	US 2002-312902	20021231
ZA 2003000024	A	20040205	ZA 2003-24	20030102
NO 2003000050	A	20030106	NO 2003-50	20030106
BG 107533	A	20031128	BG 2003-107533	20030205
HR 2003000079	A1	20030430	HR 2003-79	20030206
JP 2005002121	A2	20050106	JP 2004-206159	20040713
US 2005203165	A1	20050915	US 2005-52489	20050204
PRIORITY APPLN. INFO.:			FR 2000-8792 A	20000706
			JP 2001-584233 A3	20010706

WO 2001-FR2168 W 20010706
US 2002-312902 B1 20021231

AB The more-stable β-crystalline form of the tert-butylamine salt of **perindopril** (I), characterized by its X-ray powder diffraction pattern, is prepared by refluxing the tert-butylamine salt of **perindopril** in dichloromethane, followed by cooling the mixture, and filtration. A I-contg tablet formulation is presented.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:851112 HCAPLUS
DOCUMENT NUMBER: 135:371631
TITLE: Preparation and X-ray characterization of the ACE-inhibiting α-crystalline form of the tert-butylamine salt of **perindopril**
INVENTOR(S): **Pfeiffer, Bruno; Ginot, Yves-Michel ; Coquerel, Gerard; Beilles, Stephane**
PATENT ASSIGNEE(S): Les Laboratoires Servier, Fr.
SOURCE: PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001087835	A1	20011122	WO 2001-FR2167	20010706
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2811320	A1	20020111	FR 2000-8793	20000706
FR 2811320	B1	20020823		
CA 2415438	AA	20011122	CA 2001-2415438	20010706
EP 1296947	A1	20030402	EP 2001-954058	20010706
EP 1296947	B1	20040204		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001012367	A	20030513	BR 2001-12367	20010706
JP 2003533507	T2	20031111	JP 2001-584232	20010706
JP 3602826	B2	20041215		
AT 258918	E	20040215	AT 2001-954058	20010706
NZ 523173	A	20040430	NZ 2001-523173	20010706
PT 1296947	T	20040531	PT 2001-954058	20010706
EE 200300001	A	20040816	EE 2003-1	20010706
ES 2214434	T3	20040916	ES 2001-1954058	20010706
ZA 2002010092	A	20031212	ZA 2002-10092	20021212
US 2003186896	A1	20031002	US 2002-312961	20021231
NO 2003000024	A	20030103	NO 2003-24	20030103
BG 107532	A	20031231	BG 2003-107532	20030205
HR 2003000077	A1	20030430	HR 2003-77	20030206

US 2005059609	A1	20050317	US 2004-792355	20040303
JP 2005047902	A2	20050224	JP 2004-206158	20040713
PRIORITY APPLN. INFO.:			FR 2000-8793	A 20000706
			FR 2000-8973	A 20000706
			JP 2001-584232	A3 20010706
			WO 2001-FR2167	W 20010706
			US 2002-312961	B1 20021231

AB The α-crystalline form of the ACE-inhibiting tert-butylamine salt of **perindopril** (I) is prepared by refluxing the tert-butylamine salt of **perindopril** in Et acetate, cooling the mixture, and filtering the I α-crystal modification, which is characterized by its powder X-ray diffraction pattern, and a I-containing pharmaceutical formulation is prepared

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:816626 HCAPLUS
DOCUMENT NUMBER: 135:344373
TITLE: Process for preparing the novel γ crystalline form of the diuretic **perindopril** tert-butylamine salt
INVENTOR(S): **Pfeiffer, Bruno**; **Ginot, Yves-Michel** ; **Coquerel, Gerard**; **Beilles, Stephane**
PATENT ASSIGNEE(S): Adir et Compagnie, Fr.
SOURCE: PCT Int. Appl., 11 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001083439	A2	20011108	WO 2001-FR2169	20010706
WO 2001083439	A3	20020207		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2811318	A1	20020111	FR 2000-8791	20000706
FR 2811318	B1	20020823		
CA 2415447	AA	20011108	CA 2001-2415447	20010706
AU 2001076420	A5	20011112	AU 2001-76420	20010706
EP 1296948	A2	20030402	EP 2001-954060	20010706
EP 1296948	B1	20030910		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001012211	A	20030506	BR 2001-12211	20010706
AT 249435	E	20030915	AT 2001-954060	20010706
JP 2003531890	T2	20031028	JP 2001-580868	20010706
JP 3592296	B2	20041124		
PT 1296948	T	20031231	PT 2001-954060	20010706
ES 2206423	T3	20040516	ES 2001-1954060	20010706

NZ 523311	A	20040625	NZ 2001-523311		20010706
EE 200300003	A	20040816	EE 2003-3		20010706
US 2003158121	A1	20030821	US 2002-312903		20021231
ZA 2003000025	A	20040210	ZA 2003-25		20030102
NO 2003000051	A	20030106	NO 2003-51		20030106
BG 107534	A	20031231	BG 2003-107534		20030205
HR 2003000078	A1	20030430	HR 2003-78		20030206
HR 20030078	B1	20040630			
US 2004248817	A1	20041209	US 2004-811727		20040329
JP 2005002120	A2	20050106	JP 2004-206157		20040713
PRIORITY APPLN. INFO.:			FR 2000-8791	A	20000706
			JP 2001-580868	A3	20010706
			WO 2001-FR2169	W	20010706
			US 2002-312903	B1	20021231

AB The γ crystalline form of the diuretic **perindopril** tert-butylamine salt (I) is prepared by refluxing a chloroform-I solution, cooling the solution to 0°, and filtering the I γ crystal modification which is characterized by its X-ray diffraction pattern; a I-containing formulation is presented.

L15 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:313192 HCAPLUS
DOCUMENT NUMBER: 135:114530
TITLE: Preferential crystallisation and comparative crystal growth study between pure enantiomer and racemic mixture of a chiral molecule: 5-ethyl-5-methylhydantoin
AUTHOR(S): **Beilles, S.**; Cardinael, P.; Ndzie, E.; Petit, S.; **Coquerel, G.**
CORPORATE SOURCE: Unite de Croissance Cristalline et de Modelisation Moleculaire, SMS, IRCOF, Universite de Rouen, Mont Saint-Aignan, F-76821, Fr.
SOURCE: Chemical Engineering Science (2001), 56(7), 2281-2294
CODEN: CESCAC; ISSN: 0009-2509
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB (±)-5-Ethyl-5-methylhydantoin (12Hyd) can be separated at a preparative scale by the auto-seeded and polythermic preferential crystallization in H2O, provided that a small proportion of wetting agent was used. The influences of enantiomeric purity, supersatn. and wetting agent during the crystal growth of 12Hyd in H2O were studied. Large particles in the shape of single crystals obtained from unstirred racemic solns. and grown under smooth conditions of supersatn. exhibit unusual hourglass figures through {101} faces when observed under polarized light. Also, they contain almost no enantiomeric excess, which indicates that they are not true single crystals. This is in apparent contradiction with the possibility of resolving the racemic mixture by preferential crystallization Stereoselective dissolns. of these apparent single crystals shows that this results from a crystal growth mechanism based on the alternated 2-dimensional nucleation of homochiral domains along specific growth directions, leading to lamellar polyepitaxy phenomenon along {101} faces and responsible for the formation of hourglass figures by different types of crystal defects. Crystal structure anal. in orthorhombic space group P212121 and mol. modeling tools allow to present some explanations consistent with these data.

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:701538 HCAPLUS
DOCUMENT NUMBER: 132:100596
TITLE: Influence of a wetting agent and of the counter enantiomer on the crystal growth in water of 5-ethyl-5-methylhydantoin
AUTHOR(S): **Beilles, Stephane**; Ndzie, Elias; Cardinael, Pascal; Petit, Samuel; **Coquerel, Gerard**
CORPORATE SOURCE: Unite de Croissance Cristalline et de Modelisation Moleculaire, Universite de Rouen, MONT-SAINT-AIGNAN, F-76821, Fr.
SOURCE: International Symposium on Industrial Crystallization, 14th, Cambridge, United Kingdom, Sept. 12-16, 1999 (1999), 1175-1184. Institution of Chemical Engineers: Rugby, UK.
CODEN: 68IRAJ
DOCUMENT TYPE: Conference; (computer optical disk)
LANGUAGE: English
AB The crystal growth study of 5-ethyl-5-methylhydantoin in H2O revealed several interesting features: (i) although the title compound crystallizes as a conglomerate, single crystals grown from a racemic mixture contain almost no enantiomeric excess; (ii) crystals grown from racemic solns. exhibit systematically hourglass inclusions perpendicular to the most developed {(101)} faces; (iii) small quantities of wetting agent induce an important elongation along the main axis; and (iv) partial redissoln. expts. lead to the appearance of lamellar fragments of high enantiomeric purity. These observations are discussed from structural and modeling data.
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT